Lambert's

HISTOLOGY

AN INTRODUCTION AND GUIDE

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AN INTRODUCTION AND GUIDE

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Dedicated
to
Beginning Students in
Histology

Preface

The present revision of "Lambert's Histology" is written primarily for use as a text by beginning students in histology. It is not a reference book and, for this reason, controversial material has been avoided as much as possible. Where differences of opinion were unavoidable, the most generally accepted opinions have been adopted. The material has been simplified and unified in an effort to aid the beginning student in learning the fundamental morphological characteristics and the functional significance of the cells, tissues, and organs of the body.

One difficulty which seems common to beginning students is the practical application of the relatively vast amount of new factual material. This becomes apparent when they attempt to identify unknown tissues and organs present in practical examinations. Short sections on methods of identification of unknowns have been included in the laboratory directions to give the student assistance in more efficiently organizing and sorting factual data for practical use.

The illustrations have been carefully revised and the number of photographs and diagrams is increased. The illustrative material has been selected in an effort to utilize only pertinent material which will better enable the student to understand and span the gap between text and slide material.

The writer expresses sincere thanks and appreciation to Dr. W. R. Ingram, Dr. W. O. Nelson, and Dr. R. G. Janes, all of the Department of Anatomy at the State University of Iowa, for their suggestions, criticisms, and help in revising the text material. The valuable suggestions given by Dr. W. M. Fowler for the chapter on blood are gratefully acknowledged. The excellent new photomicrographs would not have been possible except for the patience and splendid professional services of Mr. Jack Orris who gave generously of his time and energy to improve the quality of the illustrative material. To Mrs. John H. Grothaus the writer expresses gratitude for assistance in setting up and typing the material.

HELEN L. DAWSON

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The Microscope

It is assumed that students beginning the study of histology have received some instruction about the microscope and have had some experience in its use. Those whose acquaintance with the compound microscope is limited should become familiar with the following description of its construction and the principles on which its use is based.

The microscope is, like the analytical balances of the chemist, an instrument of precision and should be employed as such. Observations made with a microscope that is improperly used are certain to be imperfect and, therefore, untrustworthy. An elementary knowledge, at least, of the mechanical and optical principles embodied in its construction should be acquired by the student before he attempts the work of making observations with the compound microscope.

THE COMPOUND MICROSCOPE

A microscope is any lens, or combinations of lenses, by which a magnified image of an object is obtained. A single lens, or a simple combination of lenses employed for this purpose, is called a *simple microscope.* A simple microscope produces only a moderately magnified image of the object. For securing greater magnifications, a combination of lenses, or lens systems,[1] arranged in series is used. Such a combination of lenses is called a *compound microscope.*

A compound microscope (Fig. 1) consists of a mechanical part, *the stand,* and an optical part consisting of the lens systems by means of which a magnified image of the object is obtained. The optical parts are arranged in relation to an imaginary line, *the optical axis,* which extends vertically through the center of the lens systems when they are arranged in series.

THE STAND. The stand consists of a *foot* or *base* (Fig. 1, B), which is U- or V-shaped, and provides the foundation on which the microscope

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[1] A lens system usually consists of two elements, one of crown glass, the other of flint glass, their curvatures being formed so that, when they are joined together, a calculated degree of refraction of the rays of light passing through them is obtained.

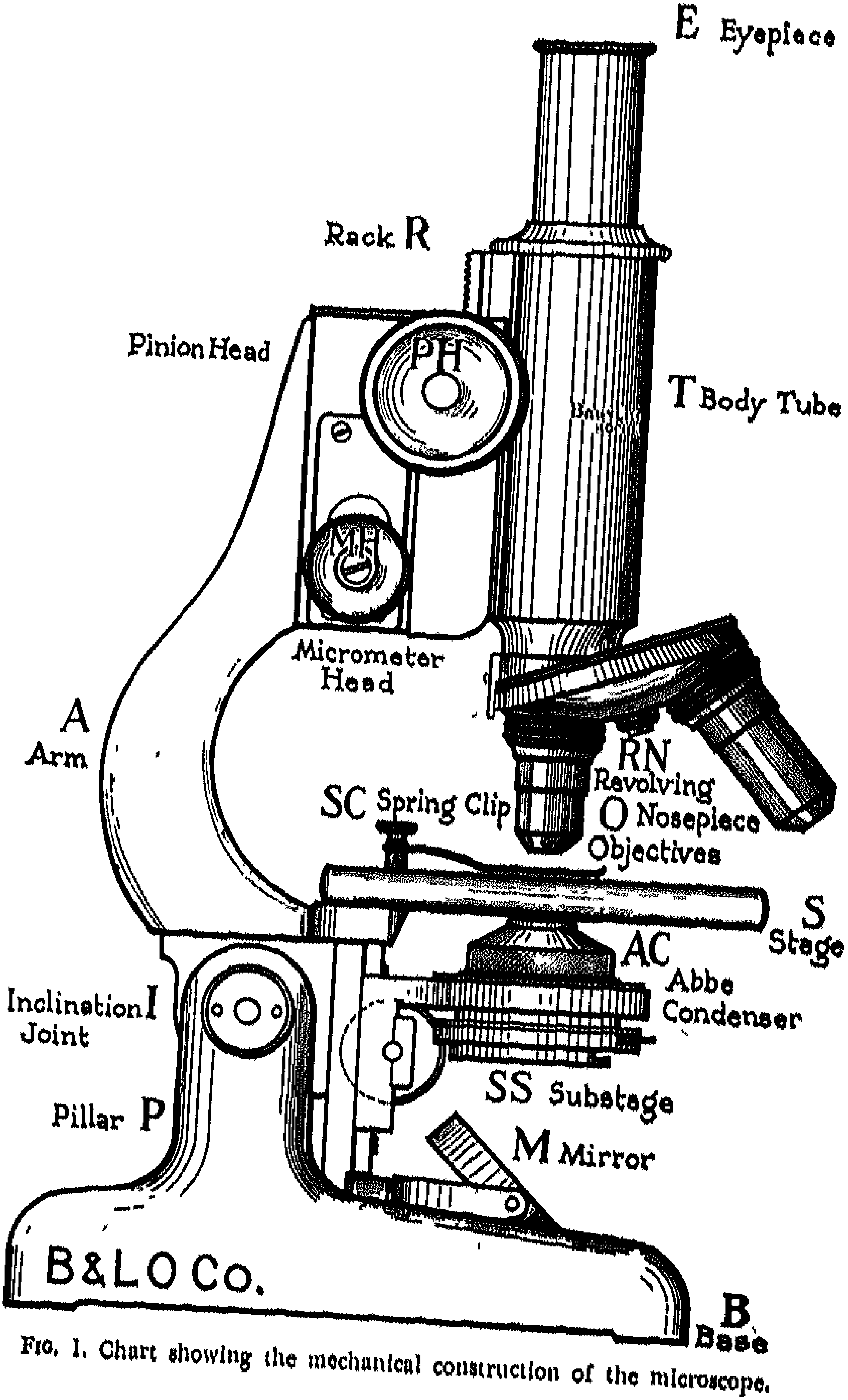

FIG. 1. Chart showing the mechanical construction of the microscope.

rests. The *pillar* (Fig. 1, P) extends upward from the foot to give support to the stage and the working parts of the instrument. The *stage* (Fig. 1, S) is a flat, rectangular or circular platform on which the object to be studied is placed. The *arm* (Fig. 1, A) continues the pillar above the stage, over which it is bent to give support to the *body tube* (Fig. 1, T) to which the optical parts are attached. The tube is a metal cylinder supported by the arm; its position above the stage is such that, when the optical parts are attached to it and are in position, they are in their proper relation to the optical axis.

The tube is attached to the arm in such a manner that it can be raised or lowered in relation to the object under observation. These movements are accomplished by two mechanisms known as the *coarse* and *fine adjustments*. The coarse adjustment consists of a rack and pinion actuated by a large, milled wheel (Fig. 1, PH) on the side of the arm. By using the coarse adjustment the long-range movements of the body tube are accomplished. It can also be used for obtaining the focal level when objectives having a low magnification are employed. The fine adjustment is a delicate mechanism operated, in the older models, by a milled wheel placed at the top of the arm or pillar. In the later models it is operated by a milled head (Fig. 1, MH) on the side of the arm. The movements of this mechanism are precise and can be used for measuring the thickness of objects under observation. Its principal use is to obtain the final focus when lenses having the higher magnification are employed.

DRAWTUBE. The drawtube is a metal cylinder which is let into the upper end of the body tube. It is used for increasing the tube length of the microscope. Most of the lens systems supplied with laboratory instruments are corrected for giving a flat field, and the least color aberration, at a tube length of 160 millimeters; therefore, in using the microscope, it is customary to set the drawtube at the line marked 160 on the graduated scale on its side.

NOSEPIECE. The nosepiece (Fig. 1, RN) consists of two circular plates, the upper of which is attached to the lower end of the body tube, the lower plate being attached to the upper plate so that it can be rotated in either direction. The objectives are attached to the nosepiece by being screwed into the places prepared for them in the lower plate. The change from one objective to another is made by rotating the plate so that as one objective is moved out, the required objective is moved into position. The objective is retained in position by a spring clip which fits into a groove on the edge of the lower plate.

THE OPTICAL PARTS. The optical parts of the compound microscope include the various systems of lenses by which light is concentrated on the object and the different degrees of magnification are obtained. They consist of *eyepieces,* or *oculars; objectives; substage* *condenser* and *mirror*. The microscope is constructed so that the optical parts, when they are in position, are in relation to an imaginary line, the *optical axis*, which passes vertically through the center of each lens in the series. If for any reason, the lens systems are not in this relation to the optical axis, the resulting image is blurred and indistinct.

OCULARS. The oculars consist of a combination of lenses which are mounted so that they can be inserted into the upper end of the draw-tube (Fig. 1, F). Two oculars are supplied with each laboratory microscope. These are marked 5 × and 10 × respectively; the number indicating the magnifying power of the ocular.

OBJECTIVES. The objectives (Fig. 1, O) are lens systems which are attached to the lower end of the body tube and provide the initial magnification. The numbers marked upon the sides of the objectives, 16 mm., 4 mm., and 1.8 mm., indicate their focal length (see p. 2).

It is customary to speak of the 16 mm. objective as the *low power;* the 4 mm. objective as the *intermediate*, or *high dry power;* the 1.8 mm. objective as the *high power*, or *oil immersion objective*. The oil immersion objectives supplied with some microscopes have a focal length of 1.9 mm. and 2.0 mm. The objective having a focal length of 1.8 mm. is the standard for making blood counts and other clinical procedure, although the objectives having the other focal lengths can be used for these purposes with equal success.

The objectives are screwed into the lower plate of the revolving nosepiece, so that each can be brought quickly into position as it is needed. The place for the attachment of each objective is usually indicated on the side of the nosepiece.

SUBSTAGE CONDENSER. The substage condenser, sometimes called the Abbe condenser after its originator, is a combination of lenses placed beneath the stage so that a maximum amount of light may be directed on the object, through which it passes to enter the objective (Fig. 1, AC). A rack and pinion mechanism (a coarsely threaded screw in some microscopes) makes it possible to raise and lower the substage condenser so that its pencil of light may be focused directly on the object when necessary.

With objectives of lower powers and wider apertures, the passage of marginal rays into the lens, which renders the image indistinct, is controlled by the *iris diaphragm*.

MIRROR. The mirror (Fig. 1, M) is attached to the substage mechanism below the condenser and is used to reflect the rays coming from the source of light, through the condenser and through the object to the objectives. The mirror is provided with a plane and a concave surface; the plane surface is to be used when the condenser is in position; the concave surface is used when the condenser has been thrown out of position, the light passing directly from the mirror to the object. Certain conditions may make it necessary to use the concave surface when the condenser is in position. The mirror is attached in such a way that it can be moved about and made to face the source from which the most suitable illumination is coming.

Optics of the Compound Microscope

To understand the principles on which the compound microscope is constructed, reference should be made to Fig. 2. The ocular (E) consists of two lenses, an eye lens (el) and a field lens (fl). The objective (O) consists of two combinations of lenses, a front combination (fc) which is toward the object, and a rear combination (rc) which is toward the body tube. The substage condenser (SC) is in position beneath the stage (S) for giving the amount of illumination required for observation with the objective used.

The slide on which the object is mounted (sl) is placed on the stage; the object being brought into position beneath the objective, which is lowered to the level necessary for obtaining the correct focus. The rays, proceeding from the source of light, are reflected from the mirror (M) and,

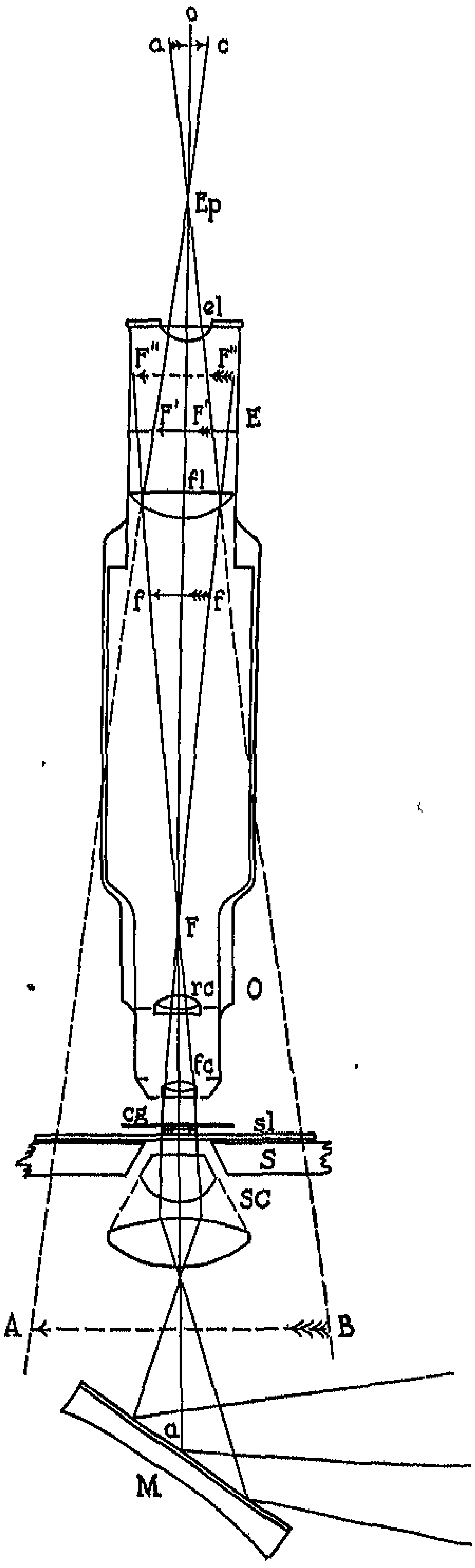

Fig. 2. Showing the pathway of the rays of light and their relation to the magnified image in the compound microscope.

passing through the substage condenser, are bent so that they converge upon the object represented by the small arrow between the cover glass (cg) and the slide (sl). From this point the rays enter the objective and, passing through its lens combinations, are bent at an angle which causes them to meet and cross at the point (F). From this point they continue until they enter the field lens of the ocular, by which they are again bent so that they pass through the aperture in the diaphragm in F′. These rays, if continued without having their direction altered by the field lens, would form an image at F″, which is out of the focal range of the eye lens (el). The rays of light, however, passing through the field lens are bent so that the image of the object is formed at F′, which is in the focal plane of the eye lens. Passing through the eye lens, the rays are directed toward the pupil of the eye (Ep), or eyepoint, from which they continue to be impinged on the retina at the plane a-c. This is the point at which the eye, when adjusted for long-distance vision (infinity), receives a clear impression of the object when the objective is in the position of exact focus.

Obviously then, instead of the eye being fatigued or strained by the effort "to see with the microscope," the proper use of the instrument requires that the eye-muscles shall be relaxed as in long-distance vision, in which the eye approximates the condition of absolute rest. In other words, a clear, visual impression of the object is obtained, not by the use of the mechanisms of accommodations of the eye, *but by the use of the focusing mechanism of the microscope.*

The impression of the image on the retina (a-c) is called the *actual image.* This image is projected along the angle of the rays entering the eye and assumes the quality of the *projected,* or *virtual, image* (A-B), which represents the magnified image of the object as seen by the observer.

TOTAL MAGNIFICATION. By following the rays of light in the diagram (Fig. 2) as they pass through the lens systems, it will be seen that, owing to their divergence, the image formed at f-f is greater than the object itself. This magnification can be understood by observing that the distance from the optical axis (o-a) to the rays which mark the margins of the image at f-f is greater than at the point where they pass through the plane of the object. This image is again magnified by the eye lens; the *total magnification* being the magnification of the image of F′-F′ (initial magnification) times the magnification of the image by the eye lens, which represents the magnification of the ocular.

These magnifications are usually marked on the lens systems. Thus, if the magnification of the objective is × 75 and that of the ocular is × 10, the total magnification will be 750 times.

RELATION OF MAGNIFICATION TO FOCAL LENGTH. There is a definite relation between the magnifying power of an objective and its focal length. The compound microscope is constructed so that the *real image* is formed in the plane *f-f*. The point where the rays meet and cross (F), on their way to form the image in the plane *f-f*, may be called the *center of focus*. The distance from the object to the center of focus is necessarily shorter in lenses of higher magnification than in lenses of lower magnification. This represents the *focal distance* of the objective. Since the focal distance in lenses of higher magnification is shorter than in those of lower magnification, the distance between the front combination of the objective and the object decreases with the increase in magnification. This is known as the *working distance* of the objective.

The focal length is marked on each objective in millimeters; 16 millimeters for the low (dry) power objective, 4 millimeters for the high (dry) power objective, and 1.8 millimeters for the oil-immersion objective.[1]

DEFINITION, RESOLVING POWER, DEPTH OF FOCUS. The performance of the compound microscope depends, not only on its magnification, but also on the three factors known as *definition, resolving power,* and *depth of focus.*

DEFINITION. Definition is the sharpness with which an object appears when the proper focal adjustments have been made. This property of an objective is assured by the care with which most modern optical equipment is constructed. If the image appears to be blurred, or indistinct, it may be assumed that the correct focus has not been obtained, or that the lenses have not been properly cleaned.

RESOLVING POWER. Resolving power is an important factor in the performance of an objective. It may be defined as the capacity of a lens to render visible two points which, when seen with a lower magnification, appear as a single point. This property of objectives is achieved by grinding the curvatures of the lenses of which they are composed, and combining their elements, so that rays of light emerging from a given point are prevented from mingling with rays emerging from an adjacent point.

The resolving power of an objective is related to, and depends upon to a large extent, a factor known as the *numerical aperture.* This is usually inscribed on the objective, the figures by which it is indicated being preceded by the letters N.A. It may be defined as the angle between the rays entering the center of the objective and those entering its outer margin. The central rays represent the lowest index of refraction of the lens; those entering its margin represent its highest index of refraction.

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[1] Attention has already been directed to the difference in the focal length of oil-immersion objectives: 1.8 mm., 1.9 mm., and 2.0 mm.

There is also a definite relation between the numerical aperture of a lens and its power of magnification: objectives having the lower numerical apertures also have the lower magnifications; those having the higher numerical apertures have the higher magnifications, and a greater resolving power as well.

This leads to the practical observation that the low power objectives give the best results when an object is being examined for its general characteristics: the higher power objectives being employed when the more minute details of structure are being sought.

The idea that the higher the magnification employed, the more one sees of the object is erroneous. The following rule should be strictly observed by the student in his use of the microscope: *Never use a magnification greater than is necessary for revealing the structures, or the parts of structures, which one wishes to observe.*

For example: in the study of an epithelium, the lower power (16 mm. objective) should be used. One is able to see, with this objective, the kind of cells of which the epithelium is formed, the number of cell layers, and, in short, the general structural characteristics of the tissue. For the study of the cells themselves, for the purpose of observing the kind of granules they may contain in their cytoplasm, the chromatin pattern of the nucleus, etc., the higher powers (4 mm., or the oil-immersion objective) should be used.

DEPTH OF FOCUS. Depth of focus or *penetration* is the capacity of a lens to reveal structures which are related to one another, but which lie at different levels. Like resolving power, depth of focus depends on the magnification and numerical aperture. Depth of focus decreases as magnifying power and numerical aperture increases.

THE OIL-IMMERSION OBJECTIVE. The principles discussed in the foregoing pages have been considered mainly in relation to that series of lenses known as "dry objectives." These objectives have a numerical aperture sufficiently low to enable them to utilize as much of the light that passes through the object as may be necessary for adequate observation without the aid of an additional refracting medium.

The numerical aperture of objectives having higher magnifications than those of the dry series is so great, and the lenses of the front combination are so small, that a considerable number of rays passing through the object are bent by refraction so that they fall outside the range of the objective. To obviate this difficulty, and to direct as large a pencil of light as possible toward the objective, a medium having the same index of refraction as that in which the object is mounted is interposed between the cover glass and the front combination of the objective.

The medium commonly used for this purpose is cedar oil of a grade especially prepared for use with the microscope. For obtaining the best result, especially in the examination of exceptionally minute objects, such as chromosomes, a drop of the oil should also be placed between the upper surface of the substage condenser and the lower surface of the glass slide on which the object is mounted.

THE SUBSTAGE CONDENSER. The substage condenser is a combination of lenses placed beneath the stage for the purpose of collecting rays as they are reflected from the mirror, so that the maximum amount of light will bear upon the object and, passing through it, enter the objective. By means of a rack and pinion, actuated by a milled wheel, the substage condenser can be raised or lowered. By this movement, the light can be regulated by focusing it on the object from below.

With objectives of low powers and wide apertures, the passage of marginal rays into the lens, causing the image to become indistinct, may be controlled by lowering the condenser to the point where the outlines of the image are clearly visible, or by closing the aperture of the iris diaphragm below the condenser until the proper degree of illumination for giving a clear image is obtained.

DIRECTIONS FOR USING THE MICROSCOPE

Having considered the principles involved in the construction of the microscope, the following suggestions for its use should be carefully observed.

1. Before attempting to use the microscope, it should be carefully examined to see that all its optical parts are thoroughly clean. Any dust that has settled on the oculars or mirror should be carefully removed. Marks, such as the impression of fingers, on any of the glass should be removed by wiping the lens with a piece of lens paper dipped in 80 per cent alcohol, after which it should be wiped again with a piece of dry lens paper.

2. Place the microscope on the desk or table so that the heel is toward the observer, the stage being directed toward the source of illumination.[1]

The instrument should never be placed so that it rests at an angle to the body of the person using it.

3. With the microscope in position, lower the 16 mm. objective to approximately the position of correct focus. Raise the condenser to its highest position beneath the stage. Open the iris diaphragm beneath the condenser to its fullest extent.

With the eye applied to the ocular, turn the plane surface of the mirror toward the source of light, manipulating it until it has caught the maximum amount of illumination and the field of vision appears to "shine" brightly. The extent of the illumination can be tested by turning the mirror, first in one direction and then in another, noting whether the field becomes brighter or dimmer as the mirror is moved about. Leave the mirror at the point where the light in the field is brightest.

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[1] These directions are for the type of microscope which is supplied students for laboratory work, or for the "physician's model." They do not apply to stands which have been designed for special kinds of research work.

A second method for illuminating the field is to remove the ocular and, looking into the tube, move the mirror about until the back combination of the objective is completely illuminated. If the illumination is greater in one part of the field, with a considerable shadow in the other part, the mirror should be moved about until the shadow has disappeared and the light is equally distributed in all parts of the lens. Close the iris diaphragm until its edges appear in the border of the field. Replace the ocular, and proceed with the examination of the object.

4. Place the slide on which the object is mounted on the stage, moving the slide about until the shadow of the object is seen in the field of vision. Be sure that the side on which the cover glass is placed is toward the objective. Fix the slide in position by placing the spring clips on either end. Lower the objective, *using the coarse adjustment,* until it is one-sixteenth of an inch, or less, above the cover glass. With the eye applied to the ocular, raise the tube slowly until the image is fairly clear. A more precise focus may be obtained by using the *fine adjustment.*

The position of the object in the field is indicated by the shadow it forms as it passes beneath the objective. When the object is too small to form such a shadow, it may be found by first focusing on the border of the label attached to one end of the slide, and then moving the slide about until the object, which will lie in almost the same focal plane as the edge of the label, is found.

When the 4-millimeter objective is to be used, the object is first found as above with the 16-millimeter objective, then changed to the higher power.

It is the policy of most manufacturers of microscopes to mount their objectives so that the approximate focal level will be the same for all. Objectives mounted in this way are said to be *parfocal.* When objectives are parfocal, one can be replaced by another without any alteration of the position of the body tube. Thus, by a simple manipulation of the revolving nosepiece, the 16-millimeter objective can be replaced by the 4-millimeter objective, or vice versa, the objective which is brought into position in this manner being approximately at the correct focal level. After this change has been made, the act of focusing is completed by using the fine adjustment. Since the numerical aperture of the 4-millimeter objective is such that a stronger illumination of the object is required, the aperture in the iris diaphragm will have to be increased with, possibly, some alteration of the position of the substage condenser.

The amount of light required for adequate observation with any objective varies with the intensity of the source from which it is obtained, and the density of the object being examined. How to obtain the amount of light which will give the best results by the manipulation of the iris diaphragm and substage condenser must be *determined by experiment.*

In case the objectives have not been mounted so that they are parfocal, the following procedure should be observed. Raise the body tube, using the coarse adjustment. Place the 4-millimeter objective in position and lower the tube until the front combination of the objective almost, but not quite, touches the cover glass. With the eye to the ocular, raise the tube very slowly until the object is visible. Use the fine adjustment for completing the focus.

Even when the objectives are parfocal, this method of obtaining the focus with the high (dry) objective is advisable, since it obviates the possibility of focusing downward, in the attempt to secure a clear image, until the focal level has been passed—which not infrequently happens—with the result that the objective crushes the cover glass spoiling a good preparation and often injuring the lens.

FOCUSING WITH THE OIL-IMMERSION OBJECTIVE

First find the object with a low magnification objective and bring it to the center of the field of vision. Raise the body tube, and bring the oil-immersion objective into position. Place a drop of cedar oil, *of the grade supplied for microscopic work,* on the cover glass above the object. Lower the body tube until the front combination of the objective is in contact with the drop of oil. Continue this movement until the lens rests *lightly* on the cover glass. Place the eye to the ocular and *raise* the tube slowly, *using the fine adjustment,* until the object is clearly in focus.

Attention has been directed to the fact that, in focusing with different objectives, the working distance of the object is lessened as the numerical aperture and degree of magnification are increased. This distance between the objective and the object may vary somewhat for different makes of objectives having the same magnification, owing to the manner in which the front combination is mounted.

The working distance of oil-immersion objectives is so slight that only a fraction of a turn of the milled head, by which the fine adjustment is operated, is necessary for obtaining the required changes of focal level.

After the object has been located and the proper focal adjustments have been made, the slide may be moved about freely since the drop of oil tends to cling to the objective.

Owing to the high numerical aperture of the oil-immersion objective, the substage condenser should be raised to its highest level and the iris diaphragm beneath it should be wide open to permit the passage of the greatest possible amount of light. The illumination of the object is greatly improved, and its finer details are more clearly observed, if a drop of the oil is placed on the upper surface of the condenser and brought into contact with the lower surface of the slide.

After using the oil-immersion objective, the oil should be removed immediately from all surfaces with which it has been in contact. If it is allowed to remain for any length of time, it hardens and can be removed *only with difficulty. Wipe the surfaces of the objective, the* slide and the condenser with a soft cloth moistened with 90 per cent alcohol, after which they should be thoroughly dried with lens paper. Xylol is sometimes used for this purpose, but this should be used with great care as it is likely to injure the mounting of the lenses.

USE OF THE FINE ADJUSTMENT

As a rule, sections are cut to a considerable degree of thickness. For this reason many important points to be observed do not lie in the same focal plane. This is especially true when the higher powers are used. That structures, or parts of structures, which lie at different levels in the same preparation may be properly observed and their relations to one another determined, it is important that these varying focal levels should be sought by a constant use of the fine adjustment. It is only as structures, as they extend from one focal level to another, are followed in this way that they can be properly observed and understood. Failure to use the fine adjustment in this manner is the mark of a poor microscopist.

CENTERING THE OBJECT

One of the difficulties most frequently encountered by the beginner in the use of the microscope is that an object, or part of an object, which has been observed with the lower power does not appear in the field when the change to an objective of a higher power is made. In microscopes whose mechanism has become somewhat worn, the recovery of this point of observation is difficult and involves a considerable loss of time. For bringing such a lost point into the field of vision the following procedure is suggested:

Using the objective of lower magnification, select some point in the section or preparation which can be readily recognized. Bring this point to the center of the field and change to the higher power. Assuming that the point selected is no longer visible in the field, select another easily identifiable point and bring it to the center of the field. Move the slide until the second point is close to the edge of the field. If the point first selected does not appear, return the second point to the center of the field and move it as before, but in a different direction. Repeat this procedure until the point first selected—which is the point sought—has been brought into the field of vision. The direction and distance of the last movement should always be used to recover a point which has passed out of the field of vision when the change has been made from one objective to another.

A permanent record of this observation should be made in the following manner: draw two circles, one to represent the field as it appears under the low power, and a second circle to show the field as it appears under the higher power (Fig. 3). Let A represent the point selected and brought to the center of the field in circle 1 (representing the low power). In circle 2 (representing the higher power) the point A lies to the right and slightly outside the field.

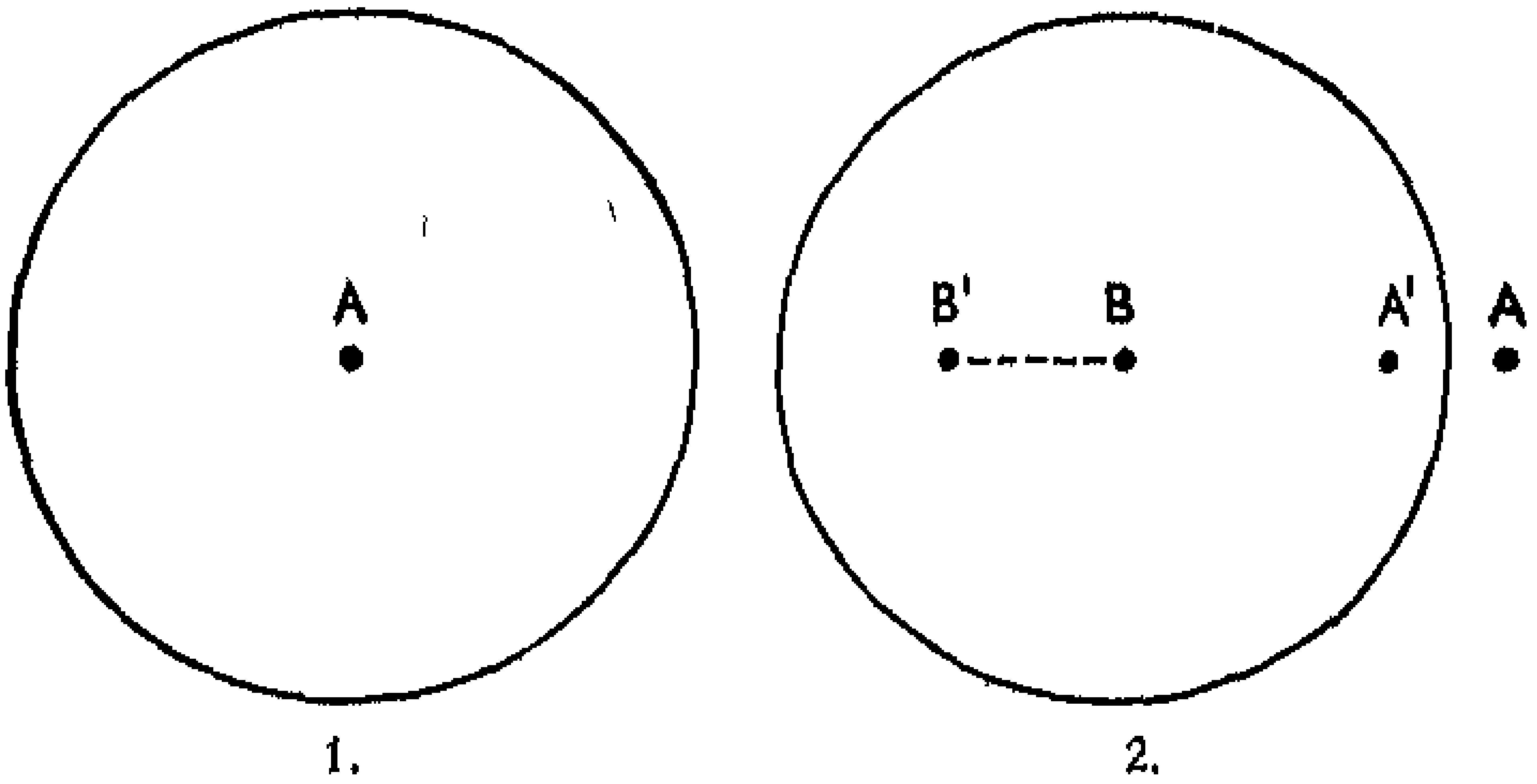

Fig. 3. Illustrating the method of bringing an object, which has been lost in changing from the low to the high objective, into the microscopic field.

Let B represent the second point selected and brought to the center of the field under the higher power. When the slide has been moved so that the point B is in the position of B′, A will appear in the field of A′.

From the foregoing, it is clear that any point centered at A under the low power objective will be out of the field when the change has been made from the lower to the higher power. Moving the slide in the direction, and through the distance, indicated by a line drawn from B to B′ will bring the object sought into the high power field, after which it is readily centered for observation.

It should be borne in mind that, in a new instrument, objects which have been centered for observation under one power will occupy nearly the same position in the field when the change has been made to another power. It is probable that only in microscopes which have been used for some time, with the development of wear in some portion of their mechanism, will the above procedure be required.

Each student should be required to find the amount of divergence between the low and high powers of the microscope he is to use by employing the above method, and make a record of that divergence. This record should be referred to whenever points selected for observation do not appear in the field of vision on changing from one objective to another.

2

The Cell

Our present information concerning the cell has been accumulated after long and painstaking studies employing a variety of techniques. At first the method most generally used was the study of dead cells and tissues. This material was prepared by first treating the tissue with a fixative, cutting it into thin sections, staining the sections and then examining them with the microscope. While this method gave a large amount of information concerning the morphology of the cell, it left much to be desired.

Since these early studies, a variety of other techniques and methods have become available and the supplementary data have in many instances verified the findings of the earlier investigators and in many instances have added entirely new information.

The methods which are currently available are:

1. Study of dead cells and tissues by means of:
   Fixed, stained sections
   Freezing-drying method
   Ultracentrifuge
   Microincineration
2. Study of living cells and tissues by means of:
   Tissue culture
   Direct microscopic examination of living tissues
   Use of vitally and supravitally stained material
   Microdissection
   Use of moving pictures taken of living cells.

For information concerning these various techniques and discussions of their advantages and limitations, the student should refer to books on techniques and to various research papers. A list of suggested reading will be found at the end of this book and students should feel responsible for availing themselves of some of these pertinent and stimulating discussions if they are to get the most out of their study of the course.

THE CELL

The cell is the vital element in the structure of all tissues. Cells are

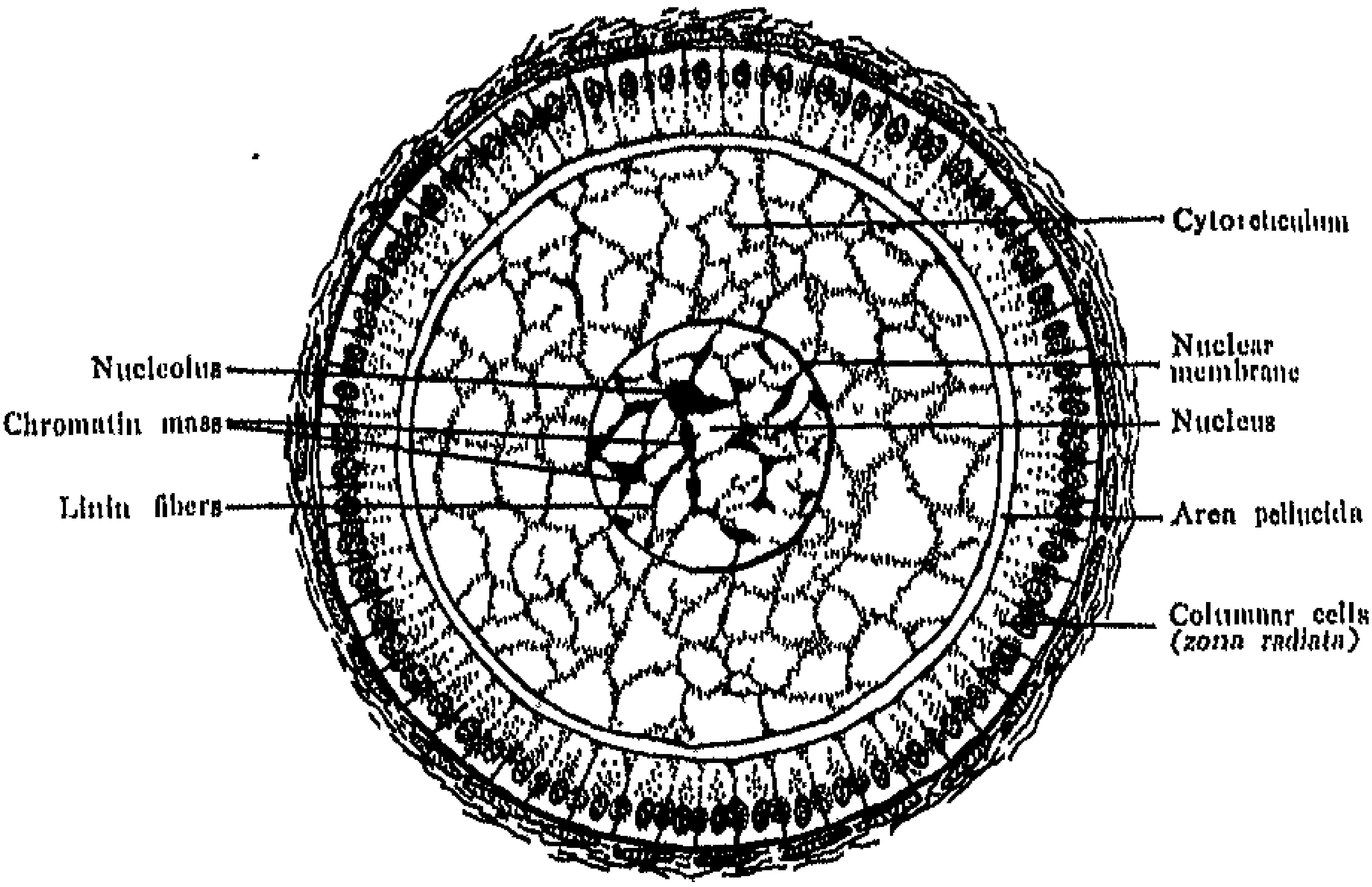

FIG. 4. Ovum. Contained in a primitive follicle in the ovary of a cat. The ovum at this stage is representative of a typical cell.

composed of a substance called *protoplasm* which in itself exhibits the important properties of growth, metabolism, irritability, and reproduction. Chemically, protoplasm consists of a relatively small number of elements, the most important of which are: carbon, oxygen, hydrogen, nitrogen, together with varying, small amounts of sulfur, iron, magnesium and phosphorus. However, these elements are combined so that the resulting substance is extremely complex. In its physical structure protoplasm belongs to that class of substances known as *colloids.*

The cell may be defined as the smallest unit of protoplasm that is capable of growth, metabolism, irritability and reproduction. Structurally it consists of two principal parts: the *cell body,* formed by protoplasm known as *cytoplasm,* and the *nucleus,* which is a smaller protoplasmic body contained within the cytoplasm of the cell body.

THE CYTOPLASM

The cytoplasm is an important part of a functional cell. This is the part of the cell which moves or contracts, thus enabling individual cells to move from place to place within tissues (wandering cells) or by its contraction makes it possible for parts of the body to move or the walls of hollow organs to contract (muscle cells). It is within the cytoplasmic portion of the cell that glandular secretions are elaborated and in nerve cells it is concerned with the transmission of impulses. There are other evidences of functional phenomena in this portion of the cell, which can be correlated with changes in appearance of certain structures contained within the cytoplasm. These will be described and discussed later.

In appearance, the cytoplasm of living cells is a clear, viscid, semifluid substance, not unlike the uncooked white of an egg. When viewed with the microscope, in fixed preparations, its appearance varies with the kind of cell and also with the stain used and the kind of fixative employed. In fixed preparations the cytoplasm usually has the appearance of being granular, although in some cells it has a characteristically homogeneous, nongranular aspect. Within it there are also other structures which may be demonstrated if the proper fixatives and stains are used in preparing the tissue. These structures are of two distinct types. The first, called *cytoplasmic organoids* are living, protoplasmic structures having definite form and they participate in the functional activity of the cell. This group includes: the *centrosome, Golgi body, mitochondria,* and *fibrils.* The second type is the *nonprotoplasmic (metaplastic) inclusions* which are more or less temporary, nonliving constituents of the cell. In this group belong *presecretion granules* (zygmogen granules), *yolk granules, fat droplets, carbohydrates* (principally in the form of glycogen), *protein accumulations,* various *pigments* and *crystalline bodies.*

ORGANOIDS: CENTROSOMES. Centrosomes have been identified in practically every animal cell, with the exception of nerve cells. When present the centrosome lies in close proximity to the nucleus, being located just external to the nuclear membrane. In a few instances it has been observed to lie within the nuclear membrane.

The centrosome consists of a spherical mass of specialized protoplasm known as the *centrosphere.* In the center of the centrosphere is a small, deeply staining body (two are present sometimes) known as the *centriole.* In cells undergoing mitotic division, delicate, filament-like rays *(astral rays)* radiate in all directions from the centrosome. The entire structure then assumes a starlike appearance and is termed an *aster.* The centrosphere and astral rays are highly resistant to ordinary staining processes, hence their substance is said to be achromatic. The centrosphere and astral rays are frequently absent from cells which are in the resting stage. For this reason the term "centrosome" is applied only to the centriole by some authors.

The centrosome plays an important part in the mitotic division of the cell and is believed by some to be concerned with the initiation of the process. In ciliated cells, bodies which are derived from the original centriole, are located at the bases of the cilia and appear to be related to their characteristic movements. These observations have led to the belief that the centriole is the center of the dynamic or energizing properties which are expressed in the movements of protoplasm.

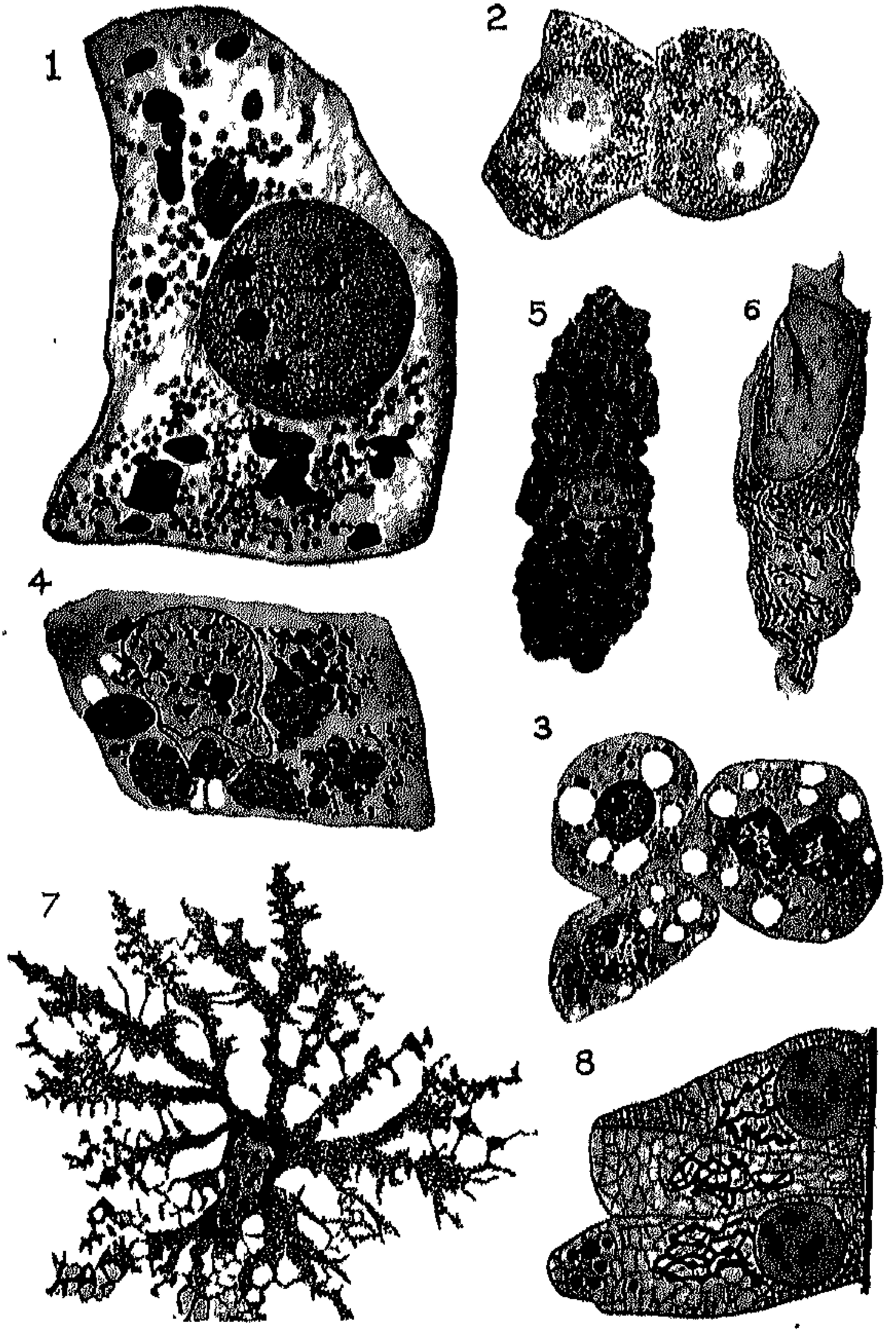

FIG. 5. Cells with various organoids and inclusions. (1) Liver cell of an axolotl. Large irregular cytoplasmic bodies are protein inclusions and smaller round bodies are *mitochondria*. The nucleus contains a round acidophil nucleolus, and granules of oxy- and basichromatin. Hematoxylin-eosin-azure stain. (1100 ×.) (2) Liver cells of a rabbit. Protein inclusions show as grey cytoplasmic areas; mitochondria as black dots. Altmann stain. (750 ×.) (3) Liver cells of a white rat; one cell is binucleate. White spaces are vacuoles resulting from dissolving of the fat. Black granules are glycogen. Fixed in alcohol and stained with Best's carmine. (800 ×.) (4) Epithelial cell, from the oral cavity of an axolotl embryo. Large irregular cytoplasmic bodies are yolk inclusions, small dots are pigment granules. Eosin-azure stain. (1200 ×.) (5) Macrophage from the subcutaneous tissue of a white rat. Round granules stained intravitally with isamine blue. (1200 ×.) (6) A *fibroblast with rod shaped mitochondria, from the subcutaneous connective tissue of a white rat.* (1200 ×.) (7) Chromatophore from an axolotl embryo. Pigment is granular black. Clear grey areas *at lower left are a few yolk granules.* (8) Golgi nets, left of nuclei, in cells *of pelvic gland of* Triton taeniatus. Within the net a few round black secretory granules are appearing. The granules near the free border of the lowest cell are from the preceding secretory cycle. Fixation Champy, stained with the Altmann method and aurantia (Figures 5 and 6 are from preparations of Tschaschin, Maximow and Bloom: "A Textbook of

Not infrequently two centrosomes are present in a cell and it is then known as a *diplosome.*

GOLGI BODY. The Golgi body (reticular apparatus: Golgi net) was first observed in nerve cells and described by Golgi in 1898. It is probably present in all cells and generally appears in the form of a fibrillar network. It is usually located in the region of the nucleus where it may be arranged in a fairly compact meshwork or it may be spread throughout a large part of the cell. Since the Golgi apparatus can be stained with osmic acid, if fixed in a fat-solvent free fixative, it is assumed that the composition of the fibrillar body is lipoidal in character. Functionally the Golgi apparatus is thought to be related to the secretory activity of the cell. This belief is based upon observations on glandular cells which show that the Golgi apparatus is increased in size during the active secretory stage of the cell and undergoes a reduction in size at the time the cell enters the resting stage. There is also evidence available which indicates that the first secretory granules formed appear within the meshwork of the Golgi apparatus. However, much still needs to be learned before the function of this structure is understood.

MITOCHONDRIA. These cytoplasmic organoids are present in all cells in the form of granular bodies, or short or long rods. They may be stained if the tissue is preserved in a fixative free of any fat solvent. This indicates their lipoidal nature. Actually they are classed as lipoproteins, in which the lipoidal portion is the minor constituent. Much speculation has arisen as to the function of the mitochondria. At present it seems probable that these structures are closely related to the secretory activity of the cell and possibly to its metabolic activity. However, the exact relationship of mitochondria to cell activity is not well understood and further critical research is necessary before this question can be satisfactorily answered.

FIBRILS. Fibrils are present in many cells, but nowhere are they as prominent as in the muscle and nerve cells. In the cells of the epidermis (prickle cells), the fibrils extend through several cells. The exact nature or function of the fibrils is not known. In muscle cells it is thought they may represent contractile elements, while in nerve cells the fibrils have been considered essential for the transmission of the nervous impulses, and in the epidermis they are thought to be important as a means of "anchoring" the cells together.

INCLUSIONS. Within the cytoplasm of cells are certain substances which are nonprotoplasmic in nature. These substances may be stored food material (yolk granules, fat droplets, glycogen granules) or they may represent waste products, resulting from the metabolic activity of the cell. Many epithelial cells show granules of pigment which are normal constituents of their cytoplasm. In other cells or under certain conditions, the presence of pigment granules is evidence of a pathologic condition.

CELL MEMBRANE. In all cells the cytoplasm is enclosed by a limiting structure known as the *cell membrane*. This membrane is an extremely important part of all cells, since it is through this membrane that substances must pass to enter or leave the cell. It is essential therefore that it be a semi-permeable membrane which functions in a selective manner, thus barring certain substances from entering or leaving the cell.

The consistency of the cell membrane varies considerably and it has been suggested that some cells have actually two membranes, first a thin, inner membrane which is formed by a modification or thickening of the cell protoplasm at the surface of the cell (plasma membrane), and secondly, a well defined cell membrane, which is readily demonstrated in many cells and which lies just external to the plasma or inner membrane. This latter membrane is readily demonstrated in certain epithelial cells and in striated muscle (the sarcolemma). It is a thin, homogeneous, structureless membrane which functions primarily as a protective enclosing layer.

The Nucleus

The nucleus is a clearly defined, basophilically staining body located within the cytoplasm. Its form varies, but tends to conform, more or less, to the general shape of the cell. In spherical or cuboidal cells the nucleus is usually spherical. In elongated cells it tends to be oval in outline. In certain specialized types of cells it may be crescentic or lobulated. In describing the appearance of the nucleus, the terms *vesicular* and *densely chromatic* are often encountered. Nuclei which are large and contain relatively small amounts of chromatin and therefore stain lightly and have an "open" appearance are said to be vesicular, to distinguish them from the smaller nuclei in which the chromatin forms a compact mass that appears as a more or less solid deeply stained body. While most cells contain a single nucleus, some of the large cells contain two or more nuclei and are known as multinuclear cells.

The nucleus contains several distinct nuclear constituents: the *nuclear membrane*, the network of *linin fibers*, and *chromatin material*, the *nucleolus*, and the *nuclear sap*.

THE NUCLEAR MEMBRANE. The nucleus is outlined by a clearly defined nuclear membrane which stains sharply with basic dyes. It is relatively thin but a fairly tough structure which serves to retain the nuclear sap and network, yet allows the nucleus to change shape if it is compressed. If it is ruptured, the nuclear sap escapes.

NUCLEAR SAP. The matrix or ground substance of the nucleus is known as the nuclear sap and in it are embedded the nuclear network and the nucleoli. It is a homogeneous, viscid, protoplasmic substance of complex chemical composition.

THE NUCLEAR NETWORK. Within the nuclear sap is a network of delicate, achromatic fibers, the *linin fibers*. Scattered along the linin fibers are masses of varying size, of a deeply staining material which is called *chromatin* because of its affinity for certain dyes. This chromatin material is probably the most important constituent of the nucleus and is intimately concerned with mitosis or cell division. Two types of chromatin are generally recognized: one, which stains with basic stains, is called *basichromatin;* the other stains with acid stains and is known as *oxychromatin*. There is evidence which seems to indicate that these two types are actually different stages of one and the same substance.

NUCLEOLI. Most nuclei contain a sharply defined spherical body, the nucleolus, which usually occupies an eccentric position in the nucleus. Cells generally contain a single nucleolus, but it is not uncommon for two or more nucleoli to be present. True nucleoli are known as *plasmosomes* and stain pink with haemotoxylin and eosin. There is another type of nucleoli which stains basophilically. These are sometimes referred to as false nucleoli or *karyosomes*. Functionally the plasmosomes are thought to be concerned with the secretory activity of the cell. Our information regarding the function of the karyosomes is more definite. These false nucleoli are unquestionably related to cell division and they serve as storehouses for the chromatin material which is required by the chromosomes during mitosis.

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THE SHAPE OF CELLS

Cells present a variety of forms. The shape of individual cells is determined by the manner in which they are grouped in tissues and also, by the nature of the function which they perform.

SPHERICAL CELLS. The egg cells (ova) of almost all animals are spherical, the principal exception being the oval-shaped eggs of certain insects. Apart from these, relatively few cells in the animal body are spherical. Certain free cells in the body fluids may assume a rounded appearance, but this form is not maintained for any considerable length of time.

POLYGONAL CELLS. Polygonal cells may be regarded as a modification of cells which are originally spherical in form. When crowded together, these cells press upon one another and the shape of adjacent cells is modified by this mutual pressure.

PYRAMIDAL CELLS. The cells which border a lumen and form the epithelial lining of certain glandular structures are pyramidal in form. This is because their basal portions, which are attached to a basement membrane, remain practically unaltered while the apical portion is compressed and narrowed.

SQUAMOUS CELLS. The types of cells which form the lining of serous cavities, blood vessels, lymph channels, some cells of connective tissues and certain cells in other localities, such as those lining the anterior chamber of the eye, appear as flattened, protoplasmic plates. Because of the extreme thinness of the protoplasmic plates, the nuclei with a small amount of cytoplasm surrounding them form a character-

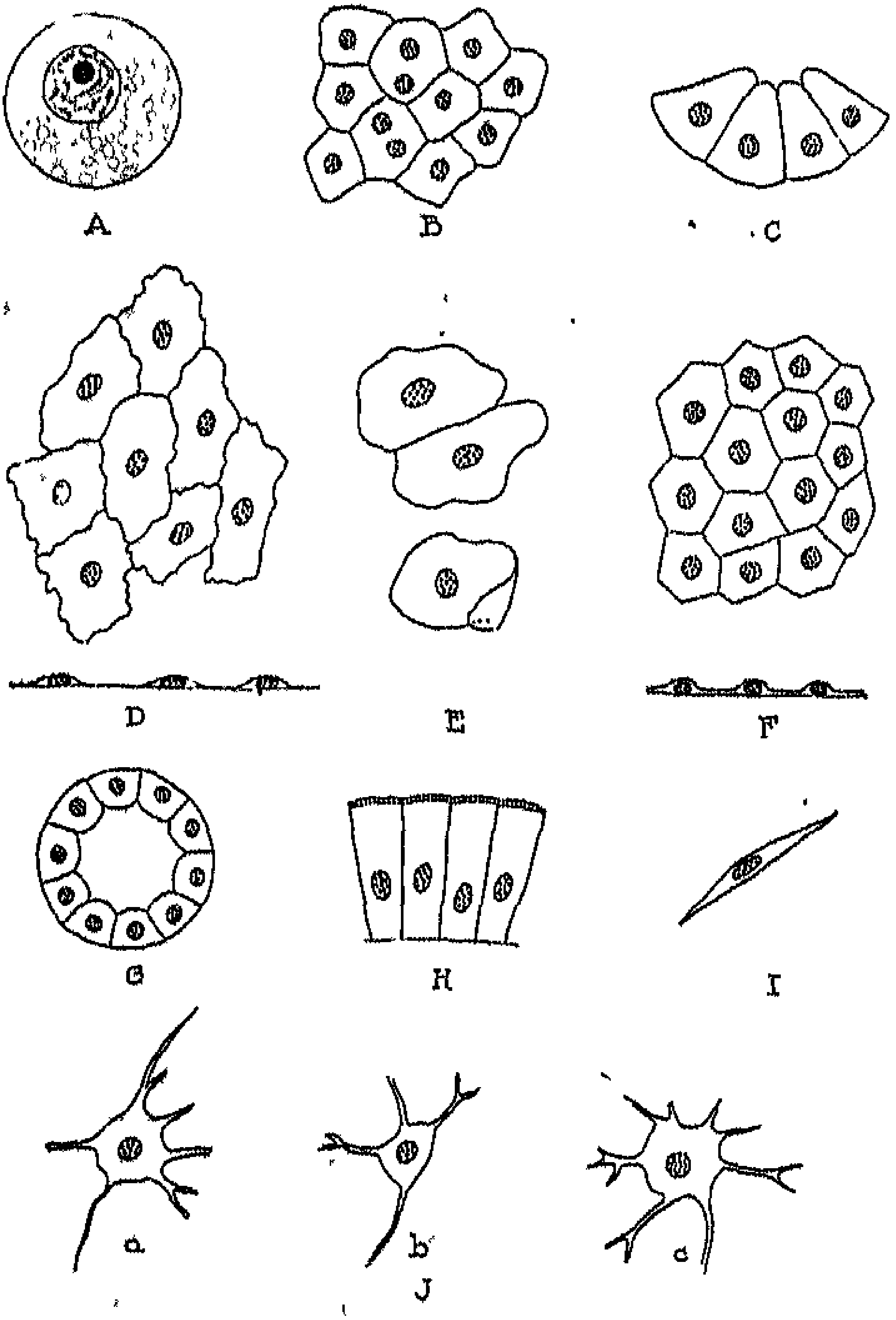

Fig. 6. Types of cells. (A) Spherical cell, ovum from ovary of dog. (B) Polyhedral cells from liver. (C) Pyramidal cells from glandular epithelium. (D) Squamous cells from mesentery. (E) Squamous cells from mouth. (F) Pavement (polygonal) cell from skin of salamander. (G) Cuboidal cells from uriniferous tubule. (H) Columnar cells from intestinal canal. (I) Fusiform cell from smooth muscle. (J) Stellate cells from central nervous system.

istic bulge when viewed in vertical (profile) section. Their scalelike appearance gives the term squamous to cells of this type.

The cells forming the outer layers of the epidermis of the skin, which have become flattened by the growth pressure of the cells beneath, are also said to be squamous.

CUBOIDAL CELLS. The cells of the epithelial lining of some of the tubules of the kidney, the smaller ducts of certain glands, etc., are equidimensional when seen in vertical section. Their nuclei are characteristically spherical and are centrally located in the cell. Such cells are said to be *cuboidal.*

Many histologists do not recognize the cuboidal form as a distinct type of cell, but regard it as a low, or depressed form of the columnar type; the difference being expressed by the terms *tall columnar, intermediate columnar* and *low columnar.* Pyramidal cells are generally regarded as a modification of the columnar cell.

COLUMNAR CELLS. Columnar cells occur in many epithelial tissues, especially in the lining of the alimentary canal. The height of cells of this type is from twice to several times their breadth, or thickness. The nuclei are usually oval in outline and are located in the basal portion of the cell.

FUSIFORM CELLS. Some of the cells associated with the connective tissues, smooth muscle cells, and cells in certain portions of the nervous system are more or less characteristically spindle-shaped. Such cells are said to be *fusiform.* In short fusiform cells the nuclei are nearly round in outline; in the longer forms they present an elongated oval appearance.

STELLATE CELLS. Cells which are provided with protoplasmic processes present an irregular outline which gives them a starlike appearance. Such cells are said to be *stellate.* Stellate cells are of frequent occurrence in the nervous tissues and in some of the earlier forms of the connective tissues.

AMORPHOUS CELLS. In the living, the shape of cells appearing in the blood, lymph and body fluids is being altered constantly by the extension and retraction of portions of the cytoplasm (pseudopodia), first in one direction and then in another. Since these cells do not present a constant form, they are said to be *amorphous* and include the cells which exhibit phagocytic properties.

CELL DIVISION

The bodies of all the higher plants and animals consist of aggregations of cells arranged in the form of tissues and organs. Since every kind of living body has its origin from a single cell, it is evident that, in the higher animals and plants, an enormous number of cells must be derived from this original cell *(ovum: germ cell)* before the final, adult form of the body is established. The process by which this increase takes place is known as *cell division.*

Cell division is a process by which a single cell is divided into two approximately equal halves, each half containing an equal amount of the cytoplasmic and nuclear material of the original cell. By this means a single parent cell becomes the progenitor of two daughter cells, each of which repeats the process after a period of growth. The formation and growth of the body is due to a continuation of this process: the cells being differentiated to form the various types of tissues which are combined to form organs, and so on until the body has attained its mature or adult condition.

Cell division is continued more or less constantly even after the adult form has been attained. With few exceptions cells in the various tissues succumb to the stress and strain of functional activity, or are destroyed by injury or disease. Wherever this loss has occurred new cells must be formed to take the place of those which have been destroyed. This process of replacement and repair is accomplished by the division of the cells that are adjacent to the worn or injured area. Under conditions which are as yet little understood, cells may be stimulated to increase at an abnormal rate, resulting in a pathological overgrowth *(hyperplasia)* of the tissue involved.

Two types of cell division are recognized: the first known as *direct cell division,* or *amitosis;* the second is called *indirect cell division,* or *mitosis.*[1]

AMITOSIS (DIRECT CELL DIVISION). In direct cell division the nucleus and cell body become elongated. A constriction appears about the middle of the nucleus, which deepens until it is divided into two approximately equal portions which separate and pass into the opposite ends of the elongated cell. The cytoplasm is likewise divided into halves by the deepening of a constriction which appears about the middle of the cell. Thus each of the two cells produced in this manner consists of one-half of the cytoplasm and one-half of the nucleus of the original cell. Before the division of the nucleus takes place, the nucleolus splits into two parts and the nucleus of each of the newly formed cells contains half of the original nucleolus.

Although the significance of amitotic cell division is not clearly understood, it appears to occur in tissues of which a more than ordinarily rapid rate of growth is required.

MITOSIS (INDIRECT CELL DIVISION: KARYOKINESIS). In this form of cell division the chromatin contents of the nucleus pass

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[1] The term, *mitosis,* is derived from a Greek word meaning *a thread.* It is applied to this form of cell division because, in the process, the chromatin assumes the form of thread-like filaments. In *amitosis* the arrangement of the chromatin in the form of filaments does not occur.

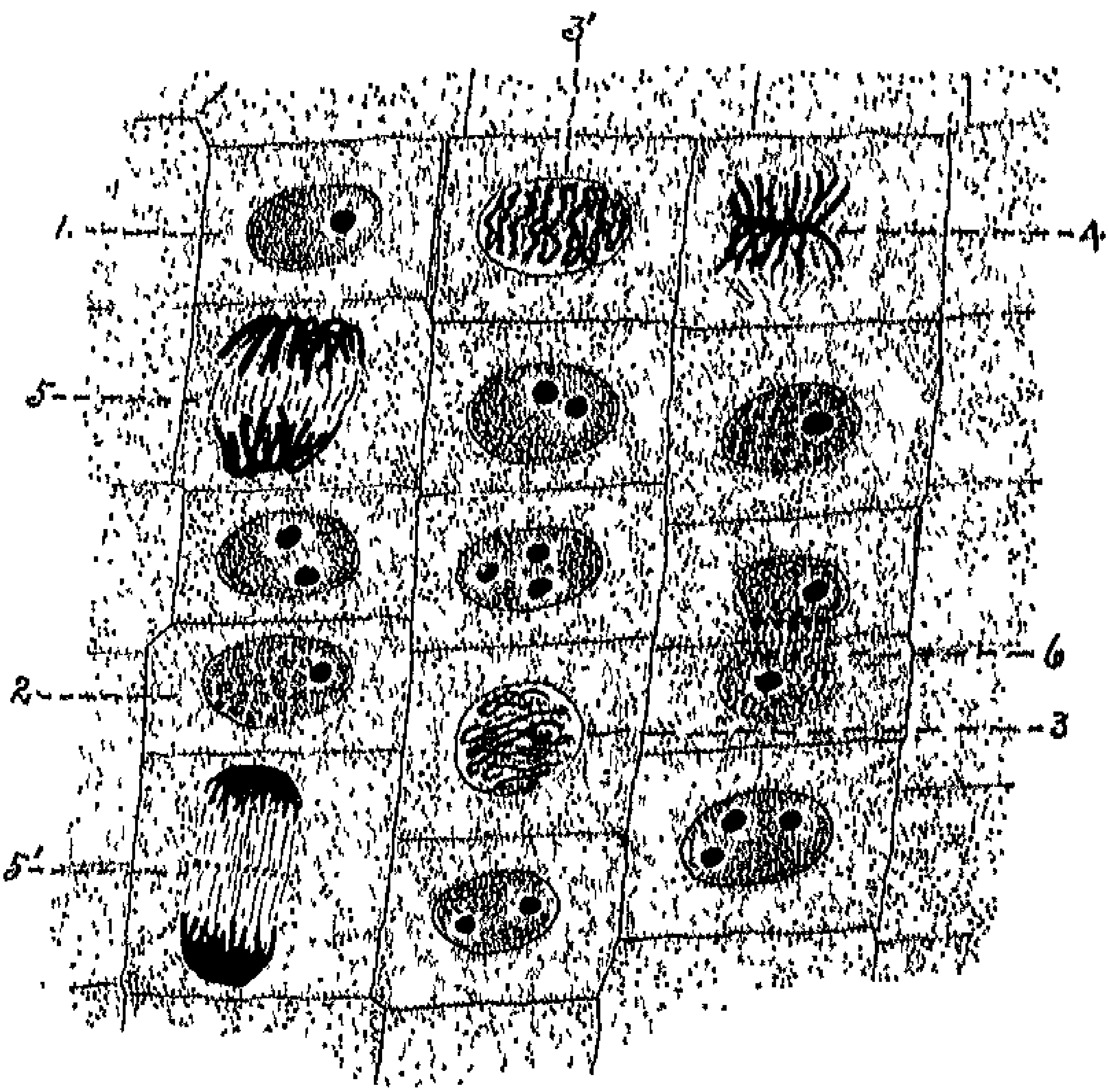

Fig. 7. Mitosis. Onion root tip. (1) Resting cell. (2) Prophase, the chromatin is grouped in small masses preparatory to the formation of the spireme. (3 and 3') Chromatin forming the ribbon-like spireme. (4) Metaphase. (5) Anaphase. (5') Later stage of anaphase. (6) Telophase.

through a series of changes, which result in an equal distribution of the nuclear material to the daughter cells. Beginning with the resting cell, these changes present a series of stages which are known as the *prophase*, the *metaphase*, the *anaphase*, and the *telophase*. While each stage refers to a certain arrangement of the chromatin bodies in the cell, mitosis should be regarded as a continuous process.

THE RESTING STAGE. The resting stage is the prelude to the mitotic division of the cell. The distribution of the chromatin in the nucleus, the position of the centrosome, and the general character of the cell corresponds to that observed in cells in which division is not taking place. Since the daughter cells, immediately after division has occurred, are smaller than the parent cells, the resting stage is to be regarded as a period of cell growth.[1]

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[1] The growth of the cell must not be confused with the growth of the body. Body growth is due to the increase in the number of cells which form its tissue constituents. Cell growth is the result of nutritional processes by which the daughter cells attain the normal size and condition of the parent cell.

THE PROPHASE. In this stage the process of division is initiated and the centrosome divides. The two centrosomes which are formed by this division move away from each other and come to rest at opposite sides of the nucleus. The achromatic fibers form rays *(astral rays)* which surround the centrosomes and the *spindle* which appears between. The chromatin material of the nucleus is assembled in the form of a coiled band or ribbon, the *spireme*. This is formed within the nuclear membrane. However, the membrane disappears and the spireme, its *coils somewhat more widely spread, comes to lie directly in relation* to the cytoplasm. With the formation of the spireme the nucleolus is lost to view.

THE METAPHASE. At the close of the prophase, the spireme is broken into a number of segments called chromosomes;[1] these assume a regular arrangement about the equator of the spindle. At the end of the metaphase the formation of the spindle is completed and each *chromosome splits longitudinally into halves.*

THE ANAPHASE. Following the metaphase, the divided chromosomes begin to move in opposite directions; one-half of each chromosome proceeding in the direction of one pole, the other in the direction of the opposite pole of the spindle.

It is believed that this movement is due to the contraction of the achromatic fibers of the spindle, some of which have become attached to the chromosomes. The *fibers attached to the middle of each chromosome apparently contract more rapidly* than those attached to the ends, this results in each chromosome being bent into a U-shaped loop, the loop being open toward the equator of the spindle.

THE TELOPHASE. At the end of the anaphase the chromosomes are assembled at their respective poles of the spindle, where they lose their identity by the apparent fusing of their chromatic substance into a single mass. They become enclosed by a new nuclear membrane which *separates the nuclear material from the cytoplasm.* A *nucleoreticulum* is formed by the arrangement of the linin fibers in a network and the distribution of the chromatin upon the fibers in the normal manner. A nucleolus appears in each of the newly formed nuclei with the nucleus resuming the appearance characteristic of the resting stage. The centrosomes which were located one at each end of the spindle are now in their usual position outside the nuclear membranes.

In the meantime a constriction has appeared about the cell body. While the changes described have been taking place, this constriction has deepened until, at the close of the telophase, the cell is divided into two halves; each half, with its newly formed nucleus, constituting a new cell.

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[1] The number of chromosomes is specific for every species of plant and animal. In one species of the roundworm, Ascaris, the number of chromosomes is two, in another species *the number is four. The number of chromosomes estimated for man is 48.*

In mitosis the chromatin granules are assembled in a linear arrangement in the *chromosomes.* The longitudinal splitting of each chromosome divides its linear components so that, as the new nuclei are formed at their respective poles of the spindle, each receives one-half of the material of which the original chromosomes were formed before the division took place. By this process each newly formed nucleus receives the dynamic elements of the original nucleus in equal proportions.

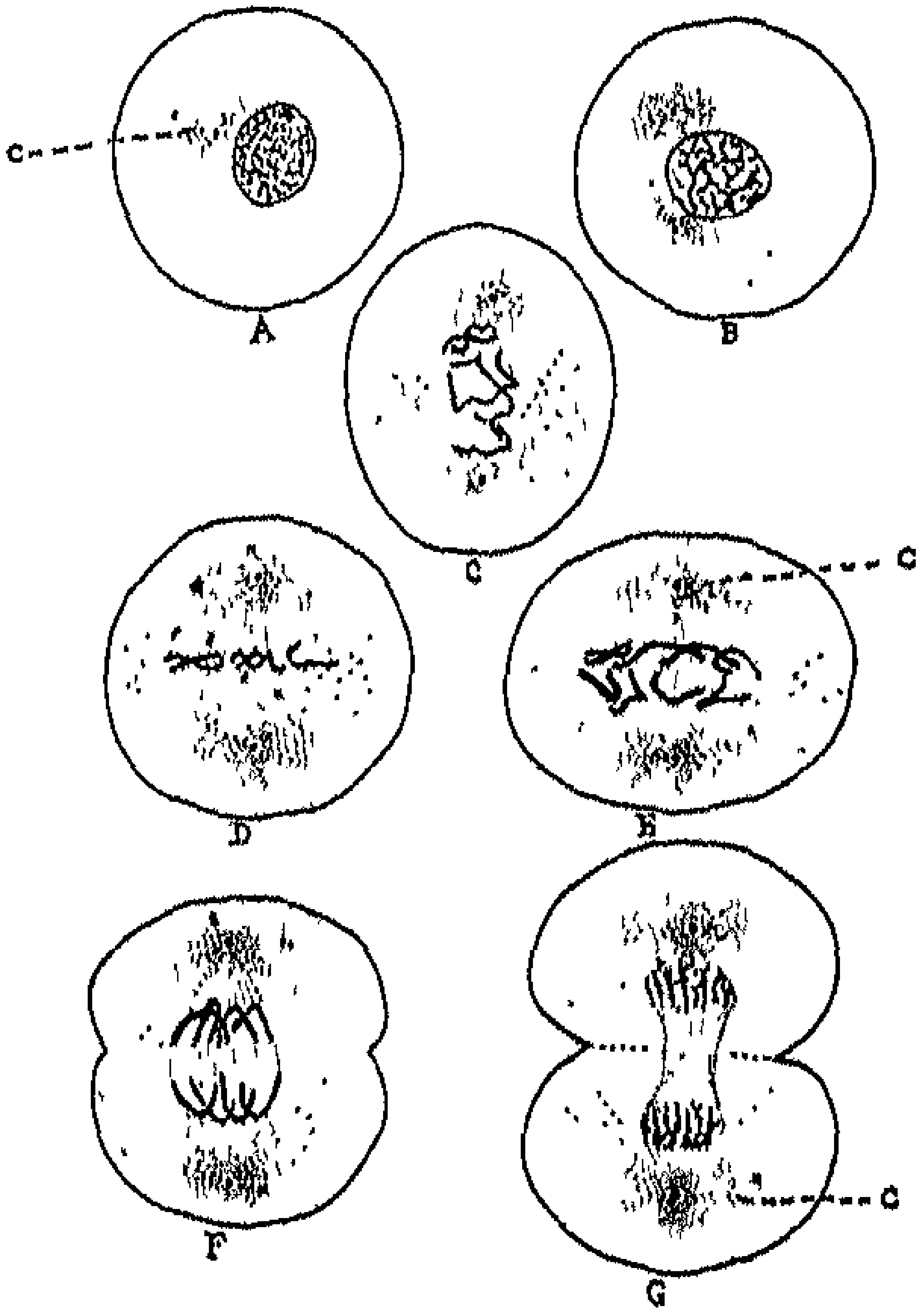


FIG. 8. Mitotic cell division. Egg-cell of Ascaris. (A) Resting stage. (B) Prophase, with division of centrosome (C). (C) Late prophase. (D) Metaphase. (E and F) Anaphase. (G) Telophase. (After Szymonowicz from Kostanecki.)

THE DIFFERENTIATION OF CELLS

As may be inferred from the foregoing discussion, all of the cells *which form the tissues of the body are derived from a single germ cell.* The cells which are first to be formed by the division of this germ cell are morphologically alike. As the number of cells increases, changes take place whereby certain groups of cells differentiate and become specialized to take over specific functional activities within the organism. One group of cells specializes to form the supportive framework of the body (connective tissues), while another group of cells takes over the transportation of food materials and elimination of some of the waste products (blood and lymph systems), etc. This functional specialization necessitates a change in the form and appearance of the cells as well as their functional capacities. This modification of form and character of the cells by which they are adapted for their place in the various tissues of the body, is known as *cell differentiation.*

Cell differentiation continues until the permanent condition of the tissue has been established. After that cells undergo division for the replacement of cells that have died as a result of functional activity, or have been destroyed by injury or disease. Thus in the fully developed organism, once differentiation has occurred, cells undergoing division produce like cells. Very few cells in the body retain their early mesenchymal potentialities whereby they can produce a variety of cell types if the need arises.

3

Epithelial Tissues

The term *epithelium* is applied to those tissues which cover the surface of the body, or form the lining of cavities and tubular structures which communicate directly or indirectly with the surface of the body.

Epithelial tissues are predominately cellular in structure, being composed of cells placed close to one another and held together by small amounts of intercellular material known as *cement substance.* This substance is soft and yielding so that the cells are not held rigidly together, but are able to change their form when yielding to pressure.

The chief function served by epithelium is protection. On the *surface of the body where it is subject to trauma, pressure, and* temperature changes, the epithelium develops its greatest protective capacity. Besides this function, it also absorbs substances as illustrated by the epithelial lining of the alimentary tract. Some of the epithelial cells in the alimentary tract differentiate to produce mucus, a thick viscid secretion which serves to protect the epithelium from being autolysed by digestive juices and to act as a lubricating material throughout the intestine. The functions required of epithelial tissues necessitate a capacity for regeneration and repair, which they exhibit to a marked degree.

In some types of epithelium, as in certain areas in the epidermis of the skin, the cells are separated by spaces or channels, which are filled with a lymphlike fluid. Where this occurs, the cells are joined *together by delicate extensions of their protoplasm (protoplasmic bridges).* This union of the cells is strengthened by specialized fibers *(tonofibrils)* which not only pass through the cell, but also pass from one cell to another by way of the protoplasmic bridges. The presence of these tonofibrils can be demonstrated by the use of special techniques. When these cells are separated from one another, the broken protoplasmic bridges give them a burrlike appearance, for which reason they are often referred to as *prickle cells.*

All epithelial tissues present two surfaces: a free surface and a basal surface which rests on the underlying tissue. The portion of the underlying tissue adjacent to the epithelium is usually differentiated to form a *basement membrane*. It is presumably by means of the basement membrane that the epithelium is attached to the tissue on which it rests.

The nature of the basement membrane is variously interpreted. It has been regarded as the result of the interlacing and fusion of the basal processes of the epithelial cells; as a substance secreted by the cells in which the basal processes of the cells and delicate fibers from the underlying tissues are intermingled and held together; and as a delicate network of fibers from the underlying tissue which are interwoven with the basal processes of the epithelial cells. Observations of epithelium in different areas, seem to indicate that the character of the basement membrane varies with the location and functional requirements of the tissue. The presence of a basement membrane cannot be demonstrated in relation to all types of epithelial tissues, although it, or a modification of the subepithelial tissues which serves the purpose of a basement membrane, is probably present. In the epithelium lining the respiratory tract, a well defined basement membrane is present and appears as a light staining, homogeneous zone. In the epithelium of the follicles of the thyroid gland, on the other hand, any structure resembling a basement membrane is notably absent.

KINDS OF EPITHELIAL TISSUES

The kinds of epithelial tissues are recognized and classified according to the *shape* of their cells (*squamous, cuboidal* or *columnar*) and by

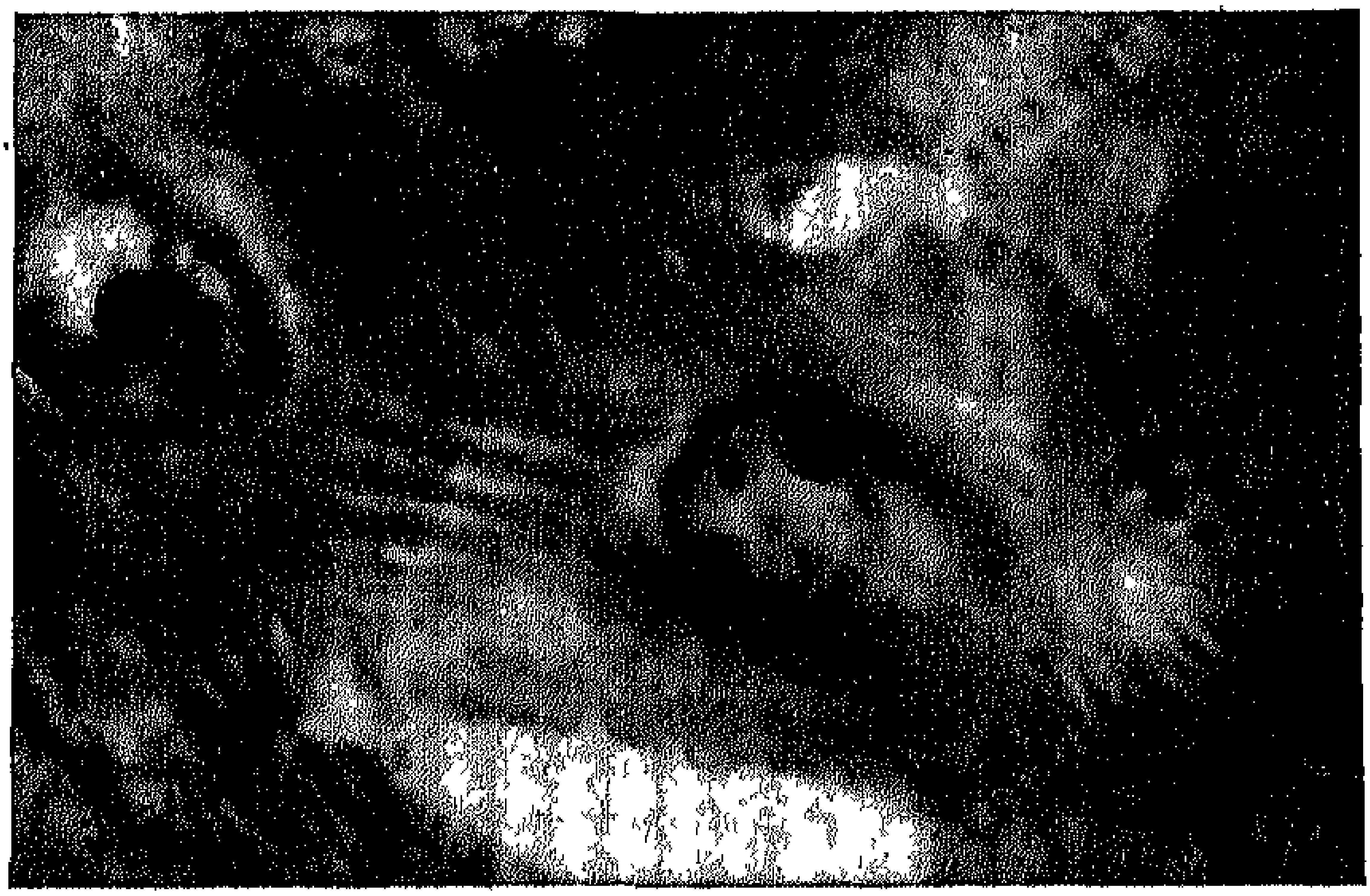


FIG. 9. Epithelial cells in the lower layers of human stratified epithelium to show protoplasmic bridges and tonofibrils. (Photomicrograph copyrighted by General Biological Supply House, Chicago.) (Courtesy, Cole: "Textbook of Comparative Histology," Philadelphia, The Blakiston Company.)

the *arrangement* of these cells in single or multiple layers (*simple* or *stratified*).

SIMPLE EPITHELIUM

A simple epithelium is one in which the cells are arranged so that they form a simple layer one cell thick. The three types of simple epithelium are: squamous, cuboidal and columnar.

SIMPLE SQUAMOUS EPITHELIUM. This type of epithelium consists of thin, flattened, plate-like cells which, when separated from the other cells of the tissue, have a scalelike appearance. The cells are closely set together, their edges being smooth or serrated as in the cells of the epitheloid tissues lining the pleural and peritoneal cavities. The outline of these cells can be best demonstrated by treating with silver nitrate, since the silver is precipitated more heavily in the fluid intercellular substance than in the cells themselves. The nuclei of cells of this type are oval when seen from above. When seen in profile, these cells appear as thin plates of protoplasm, the mid-portion where the nucleus is located forms a prominent bulge on the free surface. Frequently in sections, the cells of this type of epithelium can be recognized only by the dark staining, bulging nuclei.

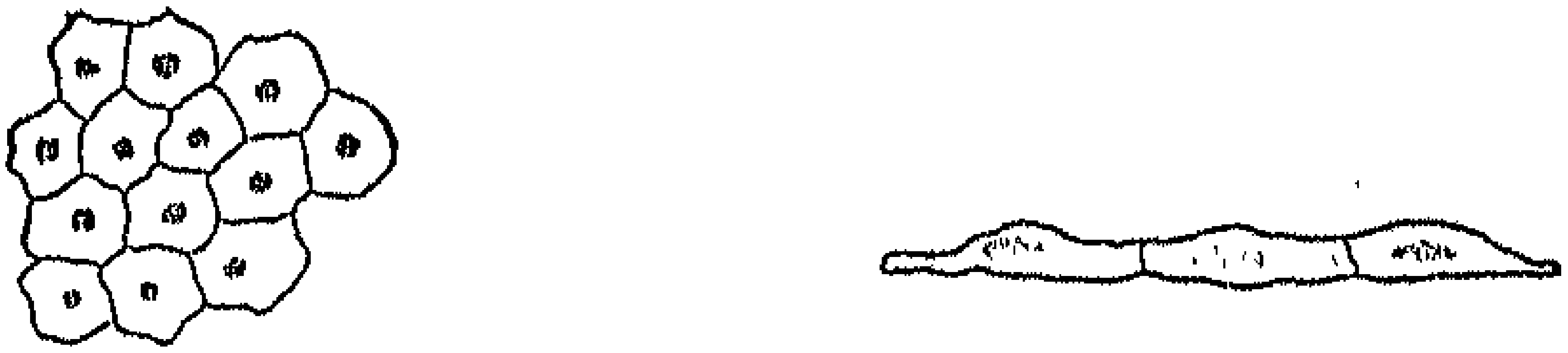


FIG. 10. Surface (*left*) and profile (*right*) views of simple squamous epithelium. (Courtesy, Stiles: "Handbook of Microscopic Characteristics of Tissues and Organs," Philadelphia, The Blakiston Company.)

Simple squamous epithelium is to be found in the capsule of the Malpighian bodies and the smaller loops of Henle in the kidney, and in the rete testis.

Specialized types of epithelial-like tissues are found lining certain cavities or spaces and vessels in the body. These specialized tissues are *mesothelium*, *endothelium*, and *mesenchymal epithelium*.

MESOTHELIUM. Mesothelium is found lining the pleural, peritoneal, and pericardial cavities. Mesothelial cells are derived from the mesoderm and are related to primitive connective tissue cells developmentally. This tissue is formed of thin, flattened cells and is similar to simple squamous epithelium in that it presents a free surface and a surface which rests on subjacent tissues. It differs from other epithelial tissue in its origin and in the manner in which it is formed. Mesothelial cells are more or less diamond-shaped with serrated edges. The nuclei are relatively small and centrally located. In profile, the cells are extremely thin and are identified by their bulging nuclei in stained sections. When mesothelium lining the body cavities is injured or destroyed, it is replaced by cells derived from the underlying connective tissue cells. Also, under proper stimuli, mesothelial cells can change into fibroblasts.

ENDOTHELIUM. Endothelium forms the lining of the entire vascular system (heart and blood vessels) and of the lymphatic vessels. Like the cells of mesothelium, these cells are derived from mesoderm. Endothelial cells are thin, flattened, relatively narrow, diamond-shaped cells. Their edges, however, are not as definitely serrated as those of the mesothelial cells. The nuclei are relatively small and centrally located. Endothelium undergoes replacement and repair only through division of other endothelial cells. However, like the cells of mesothelium, the endothelial cells can change into fibroblasts.

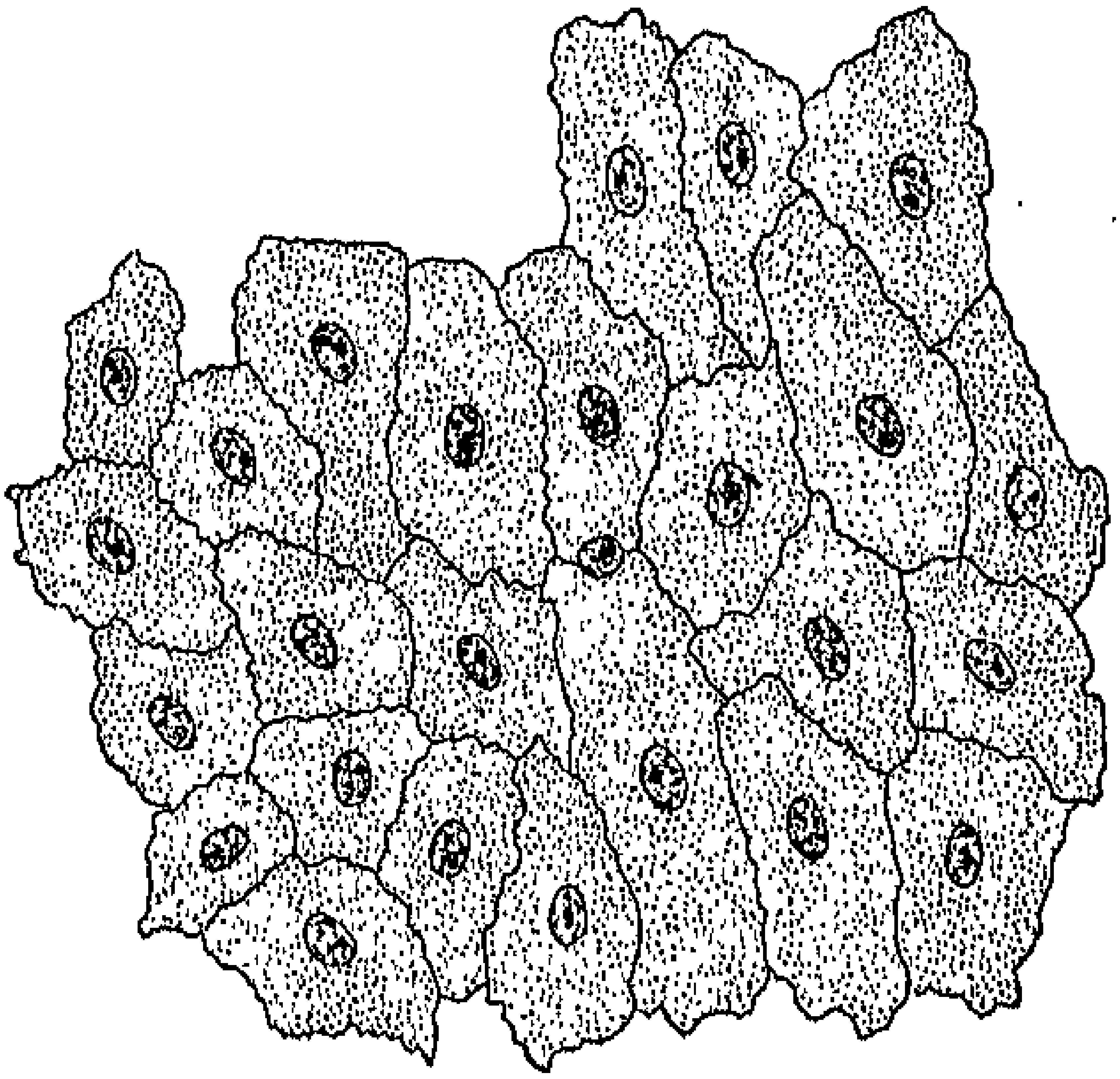


FIG. 11. Mesothelium from mesentery. Silver nitrate preparation.

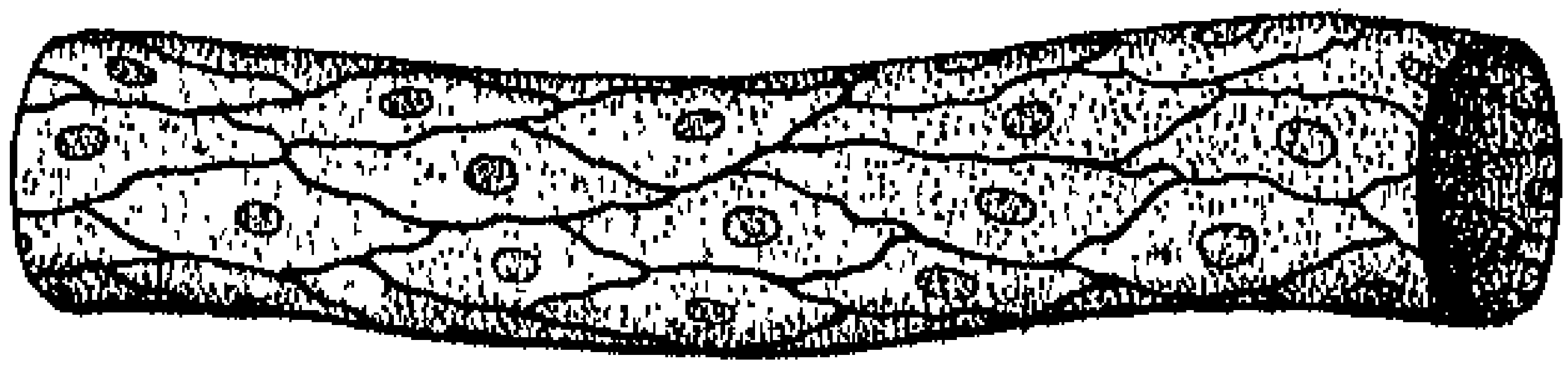


FIG. 12. Endothelial cells lining a blood vessel.

MESENCHYMAL EPITHELIUM. To indicate the tissue lining the chambers of the eye, the subarachnoid and subdural spaces, and the perilymphatic spaces of the ear, the terms *mesenchymal* or *false epithelium* are used. This tissue, which is somewhat more primitive in form than either mesothelium or endothelium, consists also of thin, flattened, squamous shaped cells. It should be remembered, however, that although they are differently named, the morphological differences between these tissues are very slight.

SIMPLE CUBOIDAL EPITHELIUM. Although many authors do not recognize the cuboidal type as a distinct form, it is a convenient term for indicating the epithelium which lines the smaller ducts in certain glands and which is to be seen in structures like the follicles of the thyroid gland.

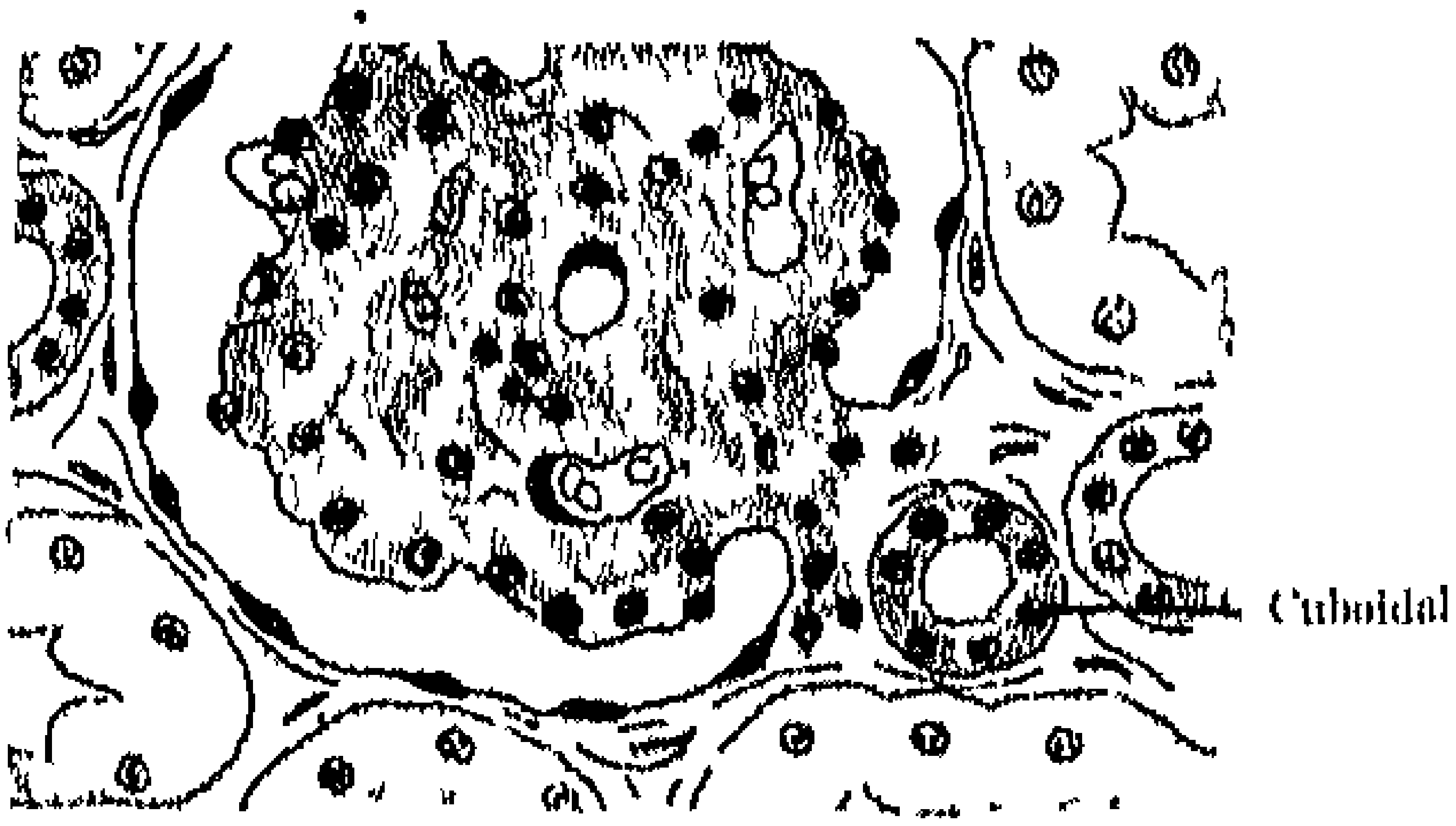


Fig. 13 Simple cuboidal epithelium from kidney.

Cuboidal cells are *equi-dimensional when seen in vertical section*, and their nuclei are spherical and located in the central portion of the cell. Cells of this type form the epithelium which lines the smaller ducts of the salivary glands and the pancreas, the bile ducts in the portal canals of the liver, certain tubules of the kidney and the undistended follicles of the thyroid gland. Cuboidal cells also appear in the basal row of most of the stratified epithelia.

SIMPLE COLUMNAR EPITHELIUM. Simple columnar epithelium is composed of tall cells, the height of which is frequently *several times their breadth*. The nuclei are *oval in outline and are* located in, or near, the basal portion of the cells. The cement substance between the cells is frequently thickened at the surface, forming a structure between the free surfaces of the cells known as a *terminal bar*. If a cell has a striated or a brush border or cilia, the terminal bars lie beneath these structures.

The free surfaces of the columnar cells which form the epithelial lining of the alimentary canal are provided with a thickened plate which, when seen in section, appears as the *cuticular plate* or *striated border*. The latter name is due to the striated appearance of this plate, the striations being minute vertical perforations or channels, through which extensions of the cytoplasm reach the surface. In view of the materials with which the free surfaces of these cells come in contact, the protective character of the cuticular plate is evident, while the vertical channels may possibly allow for an absorptive function. The free surfaces of some cells are provided with delicate, hairlike processes known as *cilia*. These cilia are not vestigial structures but are extremely important modifications of the cells on which they occur. They are surprisingly vigorous structures which persist and beat even under the most adverse conditions. Two types of cilia can be recognized: *motile cilia*, and *nonmotile* or *stereocilia*.

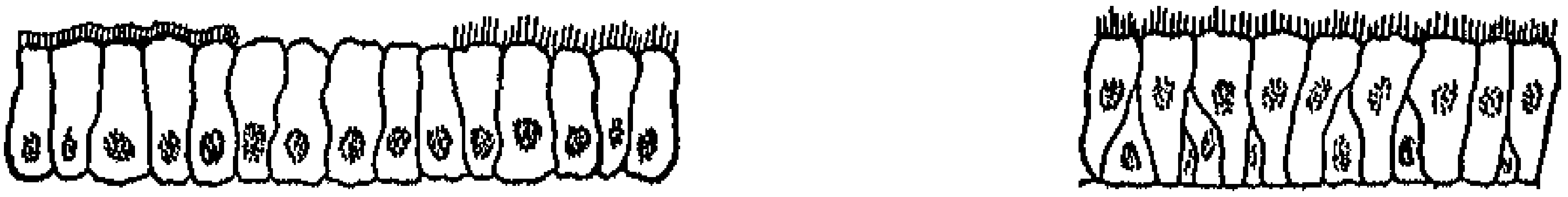


FIG. 14. Schematic representation of columnar cells showing two morphological modifications. (*Left*) Simple columnar cells at left show cuticular border; cells at right are ciliated. (*Right*) Pseudostratified columnar cells showing cilia. (Courtesy, Stiles, "Handbook of Microscopic Characteristics of Tissues and Organs," Philadelphia, The Blakiston Company.)

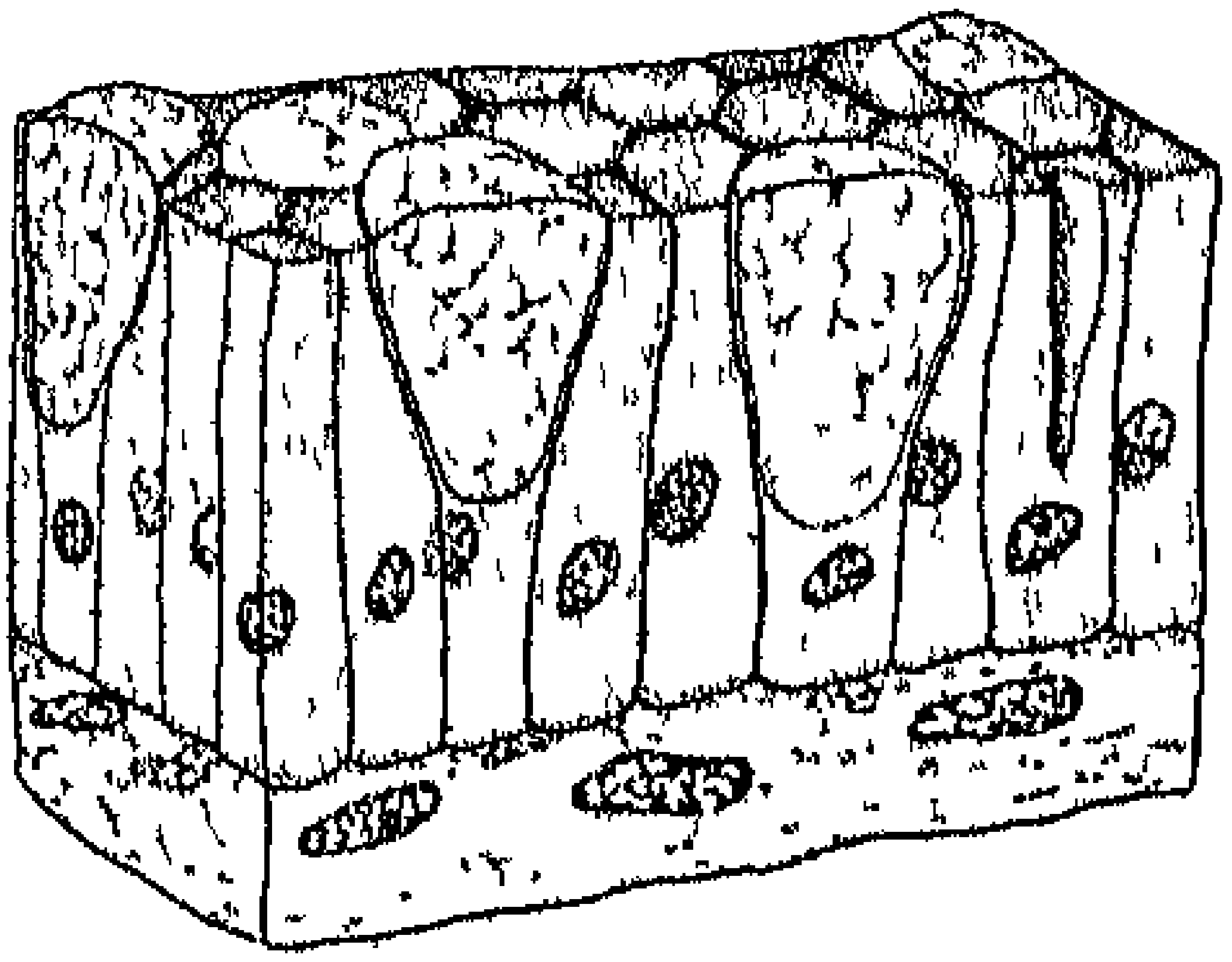


FIG. 15. Tall columnar epithelium from the intestine. Vertical section.

Motile Cilia. Motile cilia are delicate, hairlike protoplasmic processes which have the capacity for moving to and fro, the movement being stronger in one direction than in the other. At the point of attachment of the cilia to the cell, small, deeply staining, granular bodies are found within the cytoplasm of the cell, close to the cell membrane. These structures are known as *basal bodies* and in appearance they closely resemble a centrosome. The bodies are believed to have a definite relation to the ciliary movement. From these basal bodies, rootlets extend through the cytoplasm of the apical portion of the cell and end in the region of the nucleus. These rootlets are thought to be the means by which impulses are transmitted to all of the cilia of a single cell simultaneously. Structurally cilia do not show any differentiation of their protoplasm even when examined with polarized light. However, they vary in size and the rate at which they beat, depending primarily on their location. In man, the cilia in the nasal cavity are about 7 microns long and less than 3 microns wide. They are found only on moist surfaces. (In the nose, under conditions of excessive ventilation the cilia are lost.)

All cilia do not beat at the same time, but their action proceeds in a wave-like motion over the surface of the tissue. By this movement the cilia create currents in the fluids which bathe them. Since the flow is always toward the surface of the body, the cilia assist in the removal of particulate matter or small bodies from the ducts or tubes in which they are located. In the human, the frequency with which the cilia beat varies with temperature, moisture and the viscosity of the mucus covering them. The speed with which the cilia beat is not uniform even within a single organ such as the nasal cavity, but is faster where they are in a more protected region (recesses of meatuses). The speed of the streams produced by ciliary activity has been estimated to vary from .25 cm. to 75 cm. per minute. At 30° C. the cilia beat at the rate of 8–12 beats per second.

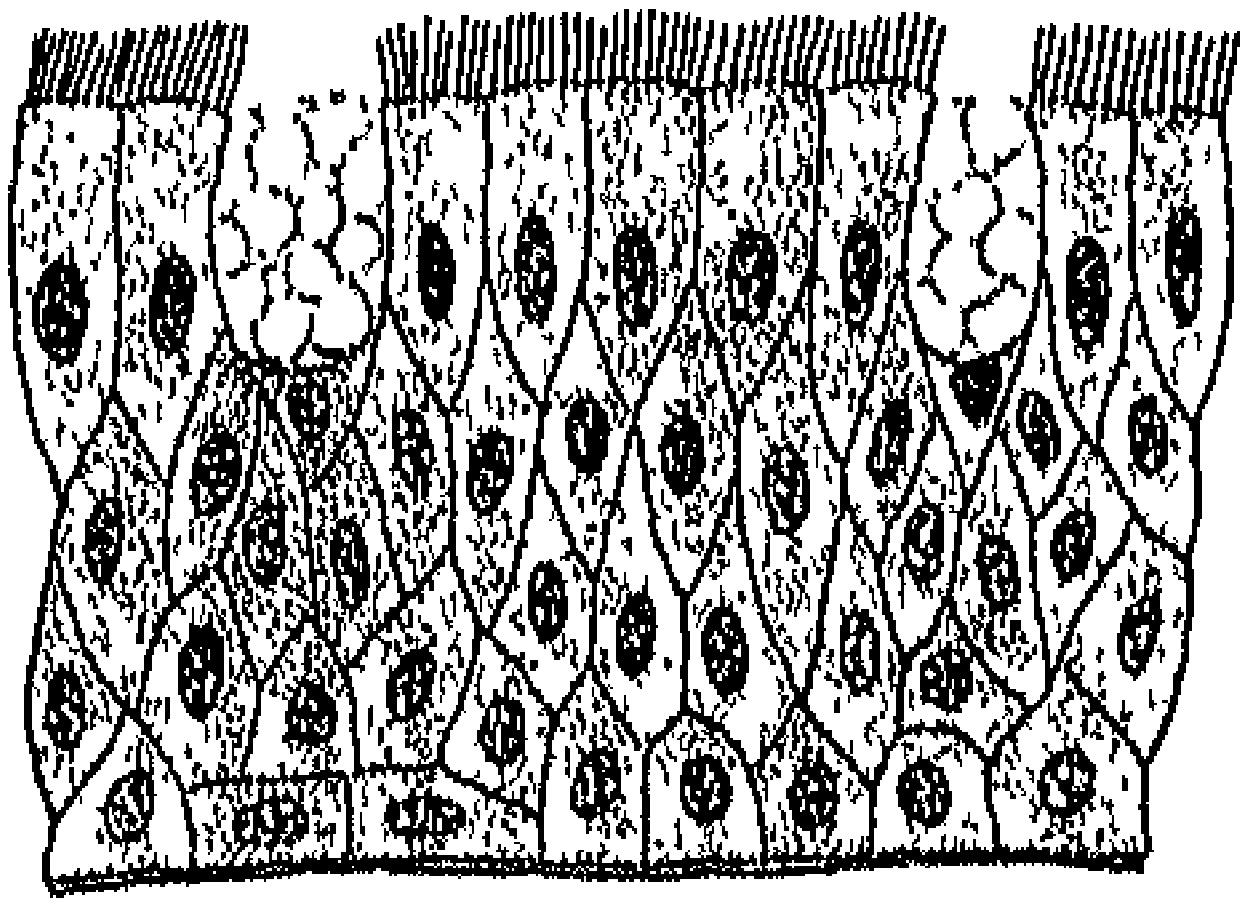


FIG. 16. Ciliated epithelial cells from the respiratory tract.

Ciliated epithelium is to be found in the nasal cavity, the trachea, the bronchi, the uterus and oviducts, the efferent ducts of the testis, the vas deferens and in the spaces of the brain and spinal cord.

NONMOTILE OR STEREOCILIA. The columnar cells found in the epididymis have long, nonmotile cilia on their free surfaces. These long hairlike cilia cling together at their distal tips and look not unlike a paint brush that has been moistened and "pointed up." These nonmotile cilia are thought to be related to the elimination of the secretion of the cells.

PSEUDOSTRATIFIED COLUMNAR EPITHELIUM. Pseudostratified epithelium is a simple columnar epithelium in which the form and position of the cells has been altered by compression, with the result that the nuclei are so arranged that the tissue has the appearance of a stratified epithelium when seen in sections. In this type of epithelium the greater number of cells are tall and narrow and extend from the basement membrane to the free surface. Between these are numerous cells which rest on the basement membrane and which extend for varying distances toward, but do not reach, the free surface. In other words the prime requisite of this type of epithelium is that every cell must reach the basement membrane, thus this epithelium can only be as thick as the height of the tallest cell. The nuclei of the tall columnar cells are oval, while those of the shorter cells are spherical. The columnar cells which reach the free surface are always provided with cilia (cilia or stereocilia).

Pseudostratified columnar epithelium forms the lining of the greater part of the respiratory tract, especially the trachea and the larger bronchi, the Eustachian tube, the epididymis and the vas deferens.

STRATIFIED EPITHELIUM

Stratified epithelial tissues are formed by the arrangement of the cells in two or more layers, the layers being superimposed one upon the other in an arrangement which closely resembles the manner in which bricks are laid in rows, one upon the other, in a wall.

Two principal types of stratified epithelium are recognized, each type being designated according to the kind of cells which form its surface layer. They are: *stratified squamous epithelium*, the surface cells of which are thin and scalelike; and *stratified columnar epithelium*, the surface layer of which consists of tall columnar cells. A third type of stratified epithelium, not designated according to the form of the cells which form its superficial layer, is known as *transitional epithelium*.

STRATIFIED SQUAMOUS EPITHELIUM. Stratified squamous epithelium consists of many layers of cells. The basal row is made up of a layer of cuboidal, or low columnar, cells which rest on the basement membrane. They are characterized by a soft, granular cytoplasm which shows considerable affinity for the basic dyes. Their nuclei are spherical and are centrally placed in the cells. The next few succeeding rows consist of polygonal cells which do not lie close together, but are separated by narrow spaces containing lymph. These spaces are crossed by protoplasmic bridges by means of which the cells *(prickle cells)* are joined to one another. The cells nearer the surface of the epithelium are more flattened, and as a result of mutual pressure, assume a fusiform shape. The loss of the granular appearance of the protoplasm and dimming of the nuclei of these cells, indicate that certain degen-

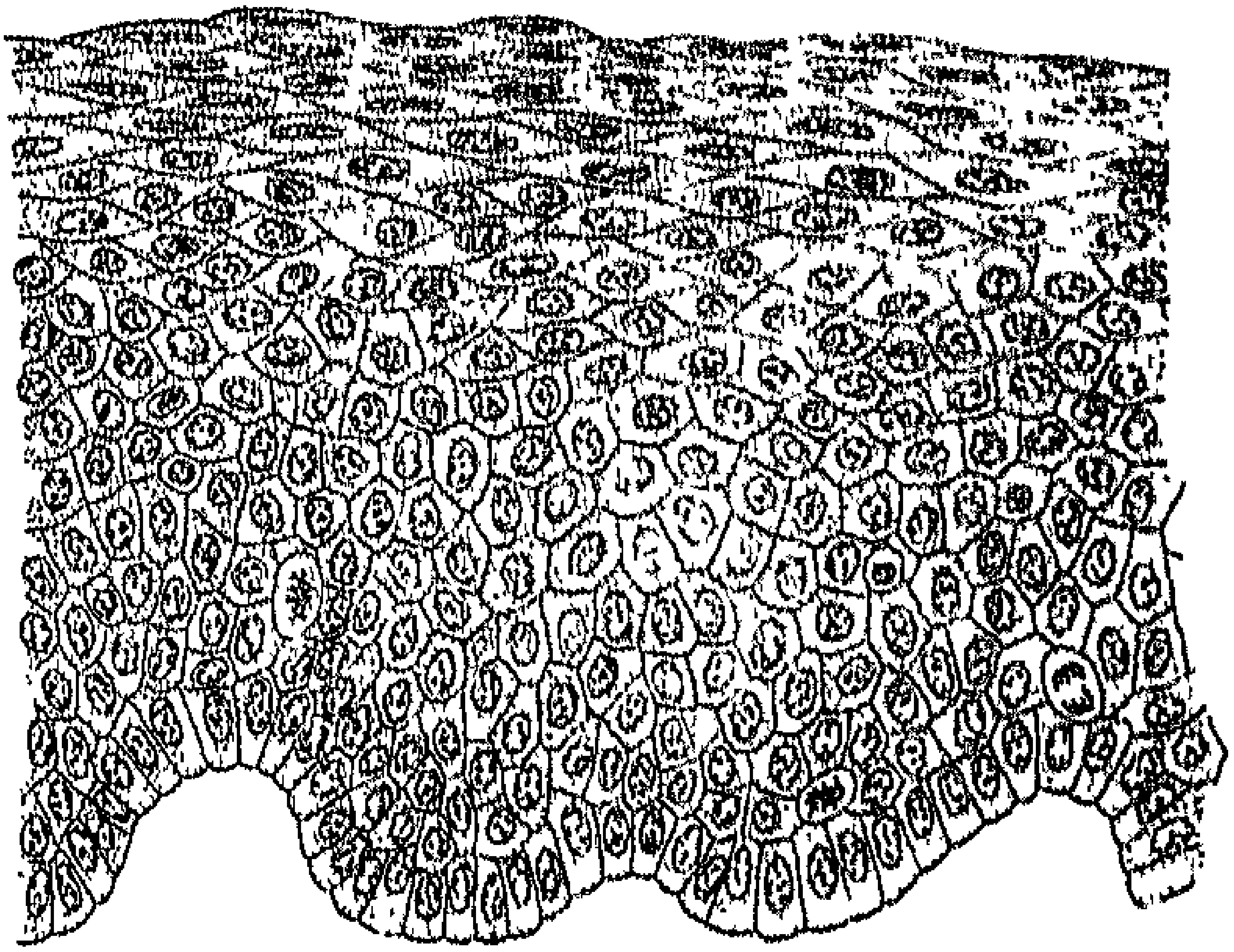


FIG. 17. Stratified squamous epithelium from lining of esophagus.

erative changes take place in the cells as they approach the surface. The cells of the superficial layers become hard through the development of a substance known as *keratin*. The cells at the surface are thin and scalelike.

As the cells at the surface of the epithelium fall off or are removed by friction *(desquamated)*, they are replaced by cells which are being more or less continually formed in the lower layers of the epithelium and pushed up from below. Mitotic figures in the cells of the deeper portion of the epithelium indicate the layers in which new cells are being formed. This area of cell proliferation is called the *stratum germinativum*.

The deep surface of a stratified squamous epithelium is rendered irregular by the upward projection of moundlike or fingerlike elevations of the subepithelial tissue. These elevations are known as *papillae*. An epithelium is said to be *papillated* when the basal line presents irregularities formed in this way. The penetration of the deep surface of the epithelium by papillae serves to establish a more adequate supply of blood and lymph vessels to the tissue, and it also enables the end sense organs to approach nearer the surface. The number and depth of penetration of the papillae may be taken as an indicator of the sensitivity of the epithelium.

The papillated basal portion of a stratified squamous epithelium helps to distinguish it from a transitional epithelium when the latter has been so stretched that its superficial cells have assumed a flattened, squamous appearance.

Stratified squamous epithelium forms the epidermal layer of the skin, the lining of the mouth, pharynx and esophagus, the conjunctiva of the eye, the lining of the external auditory canal; and it also lines the vagina and portions of both the male and female urethra.

STRATIFIED COLUMNAR EPITHELIUM. In most of the localities in which a stratified columnar epithelium was supposed to exist, more refined techniques have shown the tissue to be pseudostratified. This is especially the case with the epithelium lining the trachea and larger bronchi. There are, however, many areas in these structures where stratified columnar epithelium appears to alternate with the pseudostratified type. In some instances the entire lining of the trachea, and possibly of the larger bronchi, is very thick and appears to be true stratified columnar epithelium.

There seems to be a general agreement that the membranous urethra of the male is lined with stratified columnar epithelium.

TRANSITIONAL EPITHELIUM. Transitional epithelium is a form of stratified epithelium which lines the renal pelvis, the ureter, the urinary bladder and the first part of the urethra in both the male and the female.

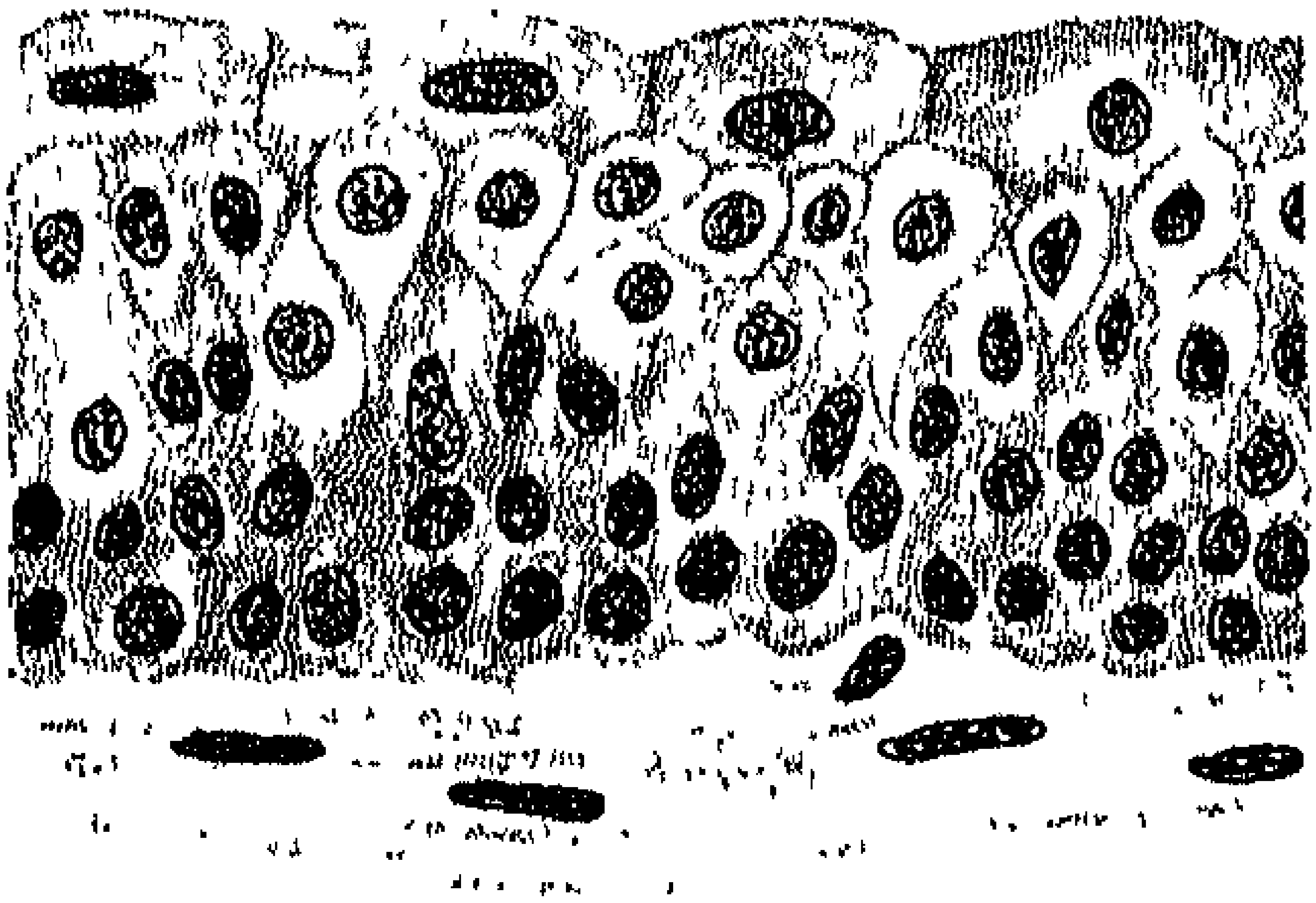


FIG. 18. Transitional epithelium from the urinary bladder

It consists of four to six rows of cells, those of the basal row being cuboidal in form. The intermediate rows consist of small, polygonal cells, while the superficial cells are more or less cuboidal, their deep surfaces being indented to receive the upper, rounded portions of the pear-shaped cells (*balloon cells*) on which they rest.

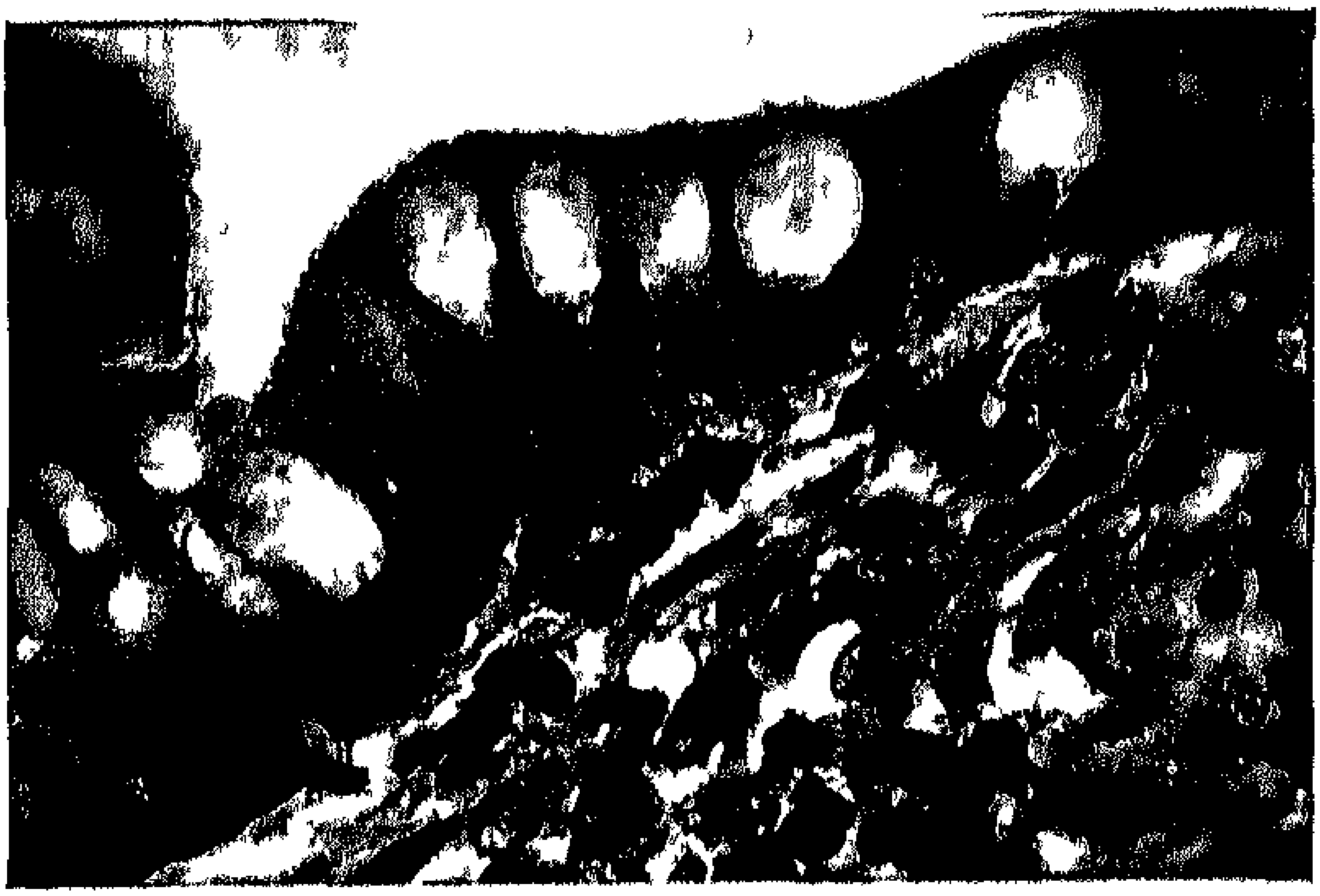


FIG. 19. Goblet cells in intestinal epithelium as seen with oil immersion. Photomicrograph.

Unlike the cells of stratified squamous epithelium, the protoplasm of all the cells of a transitional epithelium appears to be soft and granular and, hence, yielding. This enables these cells to change their form when the organs they line become distended. When distention occurs, the cells of the lower layers become compressed and smaller, while the cells of the upper layers are elongated and flattened and tend to overlap one another. In this condition the tissue resembles a thin stratified squamous epithelium.

MODIFICATIONS OF EPITHELIAL CELLS TO PERFORM SECRETORY FUNCTIONS

GLANDULAR EPITHELIUM. The cells which form the lining of glandular structures constitute the *glandular epithelium,* and are merely extensions of an epithelial tissue which has assumed a secretory function.

With few exceptions the glands are derived from one or another of the different epithelial tissues. The cells of the epithelium form structures which may persist as simple tubular invaginations (simple tubular glands), or the tubes may be extensively branched to form a system of ducts which end in tubular (alveoli) or saccular (acini) secreting bodies. These two structures, ducts and secreting endpieces, with their supporting connective tissue, form the gland.

Glandular epithelium will be discussed in further detail in the section dealing with glands as organs.

SUMMARY

DEFINITION: Epithelia are those tissues which cover the surface of the body, or line cavities or tubular structures which communicate directly or indirectly with the surface of the body. These tissues always present a free and an attached surface.

COMPOSITION:
1. Closely arranged layer or layers of cells
2. Cement substance

METHOD OF CLASSIFICATION:
1. Arrangement of cells
   - a. Simple epithelium—cells in a single layer.
   - b. Stratified epithelium—two or more layers of cells.
2. Shape of the cells
   - a. Squamous
   - b. Cuboidal
   - c. Columnar

NOTE: The identification of cells in a stratified epithelium is made by determining the shape of the cells in the free or outer layer.

EPITHELOID TISSUES: Those tissues which resemble epithelial tissues:

1. Mesothelium—tissue derived from mesoderm. It forms the lining of the pleural and peritoneal cavities.

2. Endothelium—tissue derived from mesoderm. It forms the lining of the vascular and lymphatic vessels, and the heart.

3. Mesenchymal epithelium—an epitheloid tissue derived from mesenchyme. It lines the perilymphatic spaces in the inner ear, chambers of the eye, subdural and subarachnoid spaces.

NOTE: Pseudostratified epithelium is a simple epithelium which appears to be stratified because of the arrangement of the cells.

The primary requisite of a pseudostratified epithelium is that all of the cells *must* touch the basement membrane.

CLASSIFICATION AND LOCATION OF VARIOUS TYPES OF EPITHELIA

Simple		*Stratified*	
Classification	*Location*	*Classification*	*Location*
Squamous (nonciliated)	Parietal layer of Bowman's capsule in kidney Descending limb of Henle's loop in the kidney Rete testis	Squamous	Skin Mouth Esophagus Anus Cornea Conjunctiva Vagina *Female urethra (lower part)*
Cuboidal (nonciliated)	Follicle of the thyroid gland Inner surface of the capsule of the lens *In the ducts of glands* The germinal epithelium on the surface of the ovary		
Columnar (nonciliated)	Lines the digestive tract from the gastro-esophageal junction to the recto-anal junction *Ducts of glands*	Transitional	*Only in urinary system* Pelvis of ureter Ureter Urinary bladder Upper part of urethrae (male and female)
(ciliated)	Uterus Uterine tube Nasal sinuses Small bronchi	Columnar	Upper part of anus Pharynx Ducts of some glands Male urethra (cavernous portion) Conjunctiva of fornix
Pseudostratified (nonciliated)	Ducts of some glands		
(ciliated)	Most of respiratory tract Eustachian tube Lacrimal sac		
(stereocilia)	Ductus epididymis Ductus deferens		

4

Connective Tissues (Fibrous Tissues)

Another fundamental group of tissues found throughout the body is known as *connective tissues*. As the name implies, the primary purpose of these tissues is to furnish support and form the framework for various organs and for the body as a whole. They also bind together the parts of organs.

These tissues also serve other functions. The histiocytes (connective tissue cells) aid in the defense against microörganisms that gain entrance to the body, and they also dispose of dying and disintegrating cellular elements of the body. The loose connective tissue furnishes cells for regeneration of any of the connective tissues which may be injured or damaged.

It is characteristic of connective tissues, however, that their primary functional purpose is served by their nonliving elements or fibers, rather than by their living or cellular elements. Therefore, in all of the connective tissues the fibrous elements predominate, rather than the cellular elements.

All connective tissues have three characteristics or elements in common. They are composed of: (1) *cells,* (2) *fibers,* and (3) an *intercellular ground-substance* or *matrix*. Moreover, they all originate from mesenchyme, except the reticulum of the thymus, which is derived in part at least from the endoderm. In certain other characteristics, the connective tissues differ widely from one another.

As compared with epithelium, the cells *(fibroblasts: fibrocytes)* of connective tissue appear scattered and widely separated from one another. The extent of the separation is dependent on the kind and age of the connective tissue. The cells are more numerous in the younger connective tissues than in those which have attained their mature state.

The cells are bathed or float in an intercellular substance or matrix which varies greatly in consistency. In some connective tissues, the matrix is fluid (fibrous connective tissues), it is firm and resilient in cartilage, and in bone it is dense and hard.

Fibers are also found between the cells and embedded in the matrix. Three kinds of fibers are found in connective tissue: (1) *reticular fibers*, which closely resemble collagenous fibers, (2) *collagenous* or *white fibers*, and (3) *elastic* or *yellow fibers*. All three fibers are present in all connective tissue; however, the proportion of one kind to the other two varies in each tissue, and the tissue will take the name of the predominating fiber or fibers (example: reticular connective tissue, or collagenous connective tissue).

Connective tissues may be classified in the following manner:

A. Mesenchyme—gives rise to all connective tissues
  1. Connective tissues proper
    (a) Embryonal
    (b) Reticular
    (c). Fibrous
      (1) Areolar (fibro-elastic)
      (2) Dense fibrous (tendon)
      (3) Elastic (ligamentum nuchae)
    (d) Adipose
  2. Cartilage
    (a) Hyaline
    (b) Elastic
    (c) Fibrous
  3. Bone

MESENCHYME

Mesenchyme is found in early embryos between the outer epithelial layer and the deeper structures derived from the ectoderm and endoderm. Although mesenchyme is derived mainly from the mesoderm, some embryologists claim that in one or two specific areas some of its cells may have an ectodermal or endodermal origin.

Mesenchyme consists of a delicate network of stellate-shaped cells with branching protoplasmic processes which appear to unite with one another. However, the work of Lewis (1922) offers an experimental basis for the belief that these processes merely adhere to one another at the points of contact, without definite continuity of the protoplasm of one cell with that of another. The cytoplasm of these cells is scanty and finely granular, the nucleus is large, round or oval, and occupies nearly the entire body of the cell. It is enveloped by a delicate nuclear membrane and contains only a few small granular masses of chromatin. The meshes of the cellular network are occupied by a homogeneous fluid substance or matrix.

Mesenchyme gives origin to all of the different forms of adult connective tissue, the muscular tissues, the endothelial lining of the blood

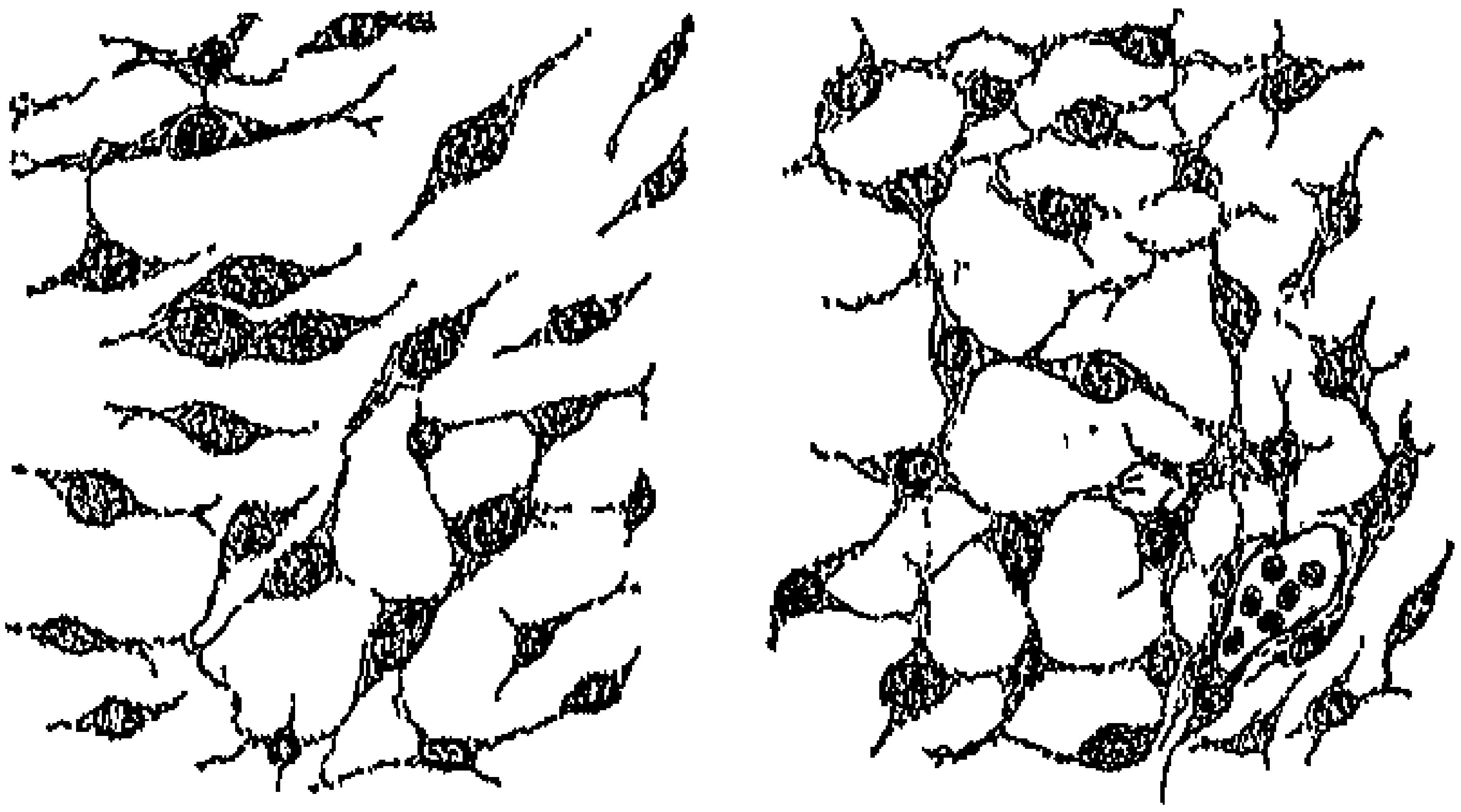

Four weeks (4.5 mm.) Sixth week (9 mm.)

FIG. 20. Drawings showing mesenchymal tissue in human embryos in two stages of development. (Courtesy, Patten: "Human Embryology," Philadelphia, The Blakiston Company.)

and lymph vessels, and the cells from which are derived the formed elements of the blood, lymph, and the bone marrow.

Mesenchyme begins to assume the definite form of a connective tissue in the later stages of embryonic development. In this process, the mesenchymal cells become larger by an increase in the amount of their cytoplasm; there is a complete or partial retraction of their processes which results in the cells assuming an irregular outline; and they become more widely separated with the more rapid growth of the embryo. Except for their increase in size and the loss of their connections with one another, the cells still closely resemble those of the original mesenchyme.

The principal change in the character of the tissue is in the appearance of numerous delicate fibers *(fibrillae)* which are interwoven in all directions in the matrix. The collagenous fibers are the first to appear, followed later by the elastic fibers. According to the age of the embryo these fibers may be single, or they may be united in the form of small fiber bundles in the older embryos.

CONNECTIVE TISSUES PROPER

EMBRYONAL CONNECTIVE TISSUE

The tissue which forms the umbilical cord, the dental pulp, and the vitreous body of the eye closely resembles the embryonic type of connective tissue. It is, in fact, the persistence of the embryonic form of connective tissue in the adult body. Tissues of this kind are often referred to as *embryonal* connective tissues to distinguish them from the tissue found in the embryo and fetus.

The connective tissue cells in the umbilical cord are elongated and irregular in outline (stellate or spindle-shaped). They retain, nevertheless, many of the characteristics of the mesenchymal cells from which they are derived. The cytoplasm is clear or finely granular and extends from the cell body in long, slender protoplasmic processes which are in contact with similar processes from other cells. The nucleus is large, oval in shape, and contains numerous fine chromatin granules. When treated with the proper stain (phosphotungstic acid hematoxylin), delicate fibrils *(border fibrils; fibroglia)* may be seen extending along the borders of the cell into the processes. However, even with the use of appropriate staining methods, these fibroglia or border fibrils have not been demonstrated consistently; therefore, they are considered by some histologists to be artefacts.

The extremely delicate fibers in the matrix are of the white or collagenous type. They are arranged in groups to form wavy fiber bundles which are located in the wide intercellular spaces. The individual fibers do not branch, but fibers or small fiber bundles may pass from one bundle to another.

The principal difference between embryonal tissue, as it appears in the umbilical cord, and the embryonic type of connective tissue, is the character of the matrix. In the umbilical cord (and also in the vitreous body of the eye) the matrix contains a mucoid substance which gives it a gelatinous consistency *(Wharton's jelly)*. Tissues in which a large amount of this substance *(mucoprotein)* is present in the matrix are known as mucoid connective tissues.

The cells of the dental pulp, with their branching processes, are more nearly like those of the original mesenchyme than are those of the other embryonal tissues. Moreover, the matrix is fluid and delicate; single fibrils extend through it in all directions.

RETICULAR CONNECTIVE TISSUE

Reticular tissue consists of a meshwork *(reticulum)* formed by the cells and their processes, and a delicate fibrillar network. These delicate fibers stain electively when treated with silver stains, for which reason they are known as *argyrophil fibers.* These reticular fibers are nonelastic, branched and joined together to form a loose network. The cells and fibers are bathed in fluid which forms the matrix of the tissue.

The reticular cells are quite primitive and appear to be only slightly differentiated from mesenchymal cells which they closely resemble. The cells are stellate in form with a light-colored, finely granular cytoplasm. The processes of the cells extend in various directions and frequently join with similar processes from neighboring cells. In some cases the protoplasmic processes are in close association with the reticular fibers, either closely applied to the fibers or encircling them. It is a question whether the fibers are extracellular, merely being in close contact with the cells, or whether they are intracellular, being in the cytoplasm at the periphery of the reticular cells.

The functional capacity and potentiality of reticular cells is varied. Two major functions can be attributed to them. First, they show definite phagocytic power as indicated by their ability to ingest certain vital dyes. When living animals are injected with coloring matter such as lithium carbonate, trypan blue, or dilute India ink in which the particles are in a finely divided state, the particles are found after a time to be taken up by the cytoplasm of the reticular cells. Cells of this kind are known as *fixed macrophages*. Under certain conditions the cells may lose their connection with the reticulum and float away in the tissue fluid, they are then known as *wandering cells*, or *true macrophages* (see reticulo-endothelial system, p. 58). Secondly, to reticular cells has been ascribed the capacity for giving rise to certain other types of cells of the blood and connective tissues.

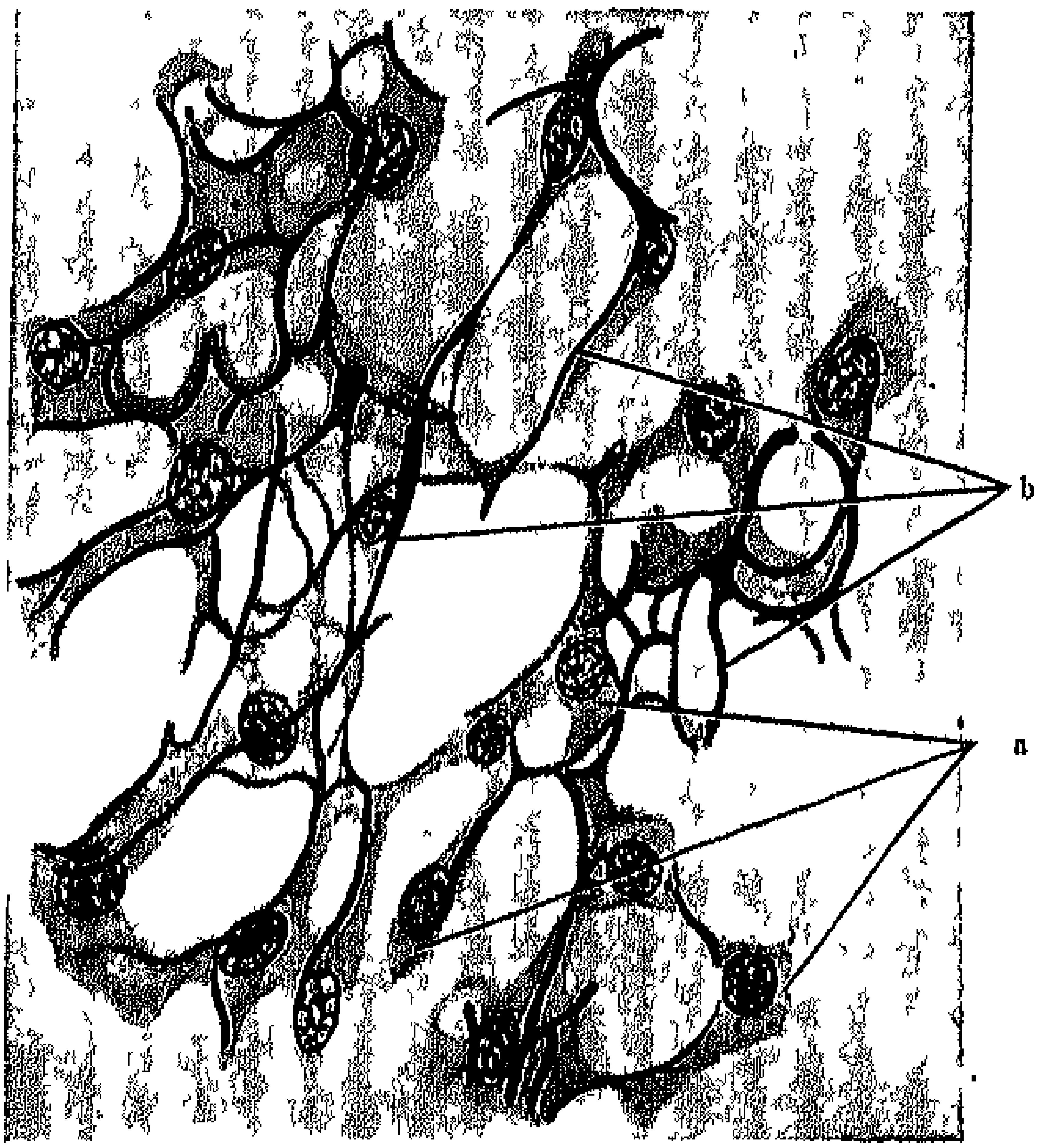


FIG. 21. Reticular connective tissue. (a) Reticular cells. (b) Reticular fibers. (Redrawn from Schäfer, after Heidenhain.)

The fibers of reticular tissue are closely related to collagenous fibers. When reticular fibers are traced into the bundles of collagenous fibers with which they are associated, they continue along with the fibers of the collagenous bundles. It seems highly probable that the argyrophilic reaction is a characteristic of collagenous fibers before they attain the mature condition. This is not only indicated by the primitive character of the cells with which they are associated, but by their distribution as well.

Reticular tissue forms the framework of the lymphoid organs, liver, and bone marrow, and is the principal subepithelial tissue of the mucosa of the alimentary canal. It is also found in the stroma of the lungs, kidneys, and many other organs. Where reticular tissue forms the support of lymph organs and in the mucosa of the alimentary tract, even though the cells and fibers cannot be distinguished in ordinary preparations, its presence is indicated by the lymphocytes which are held in its meshes. The lymphocytes can be recognized by their deeply stained nuclei, about which the cytoplasm is seen as an extremely thin border.

FIBROUS CONNECTIVE TISSUE

The distinctive characteristic of fibrous connective tissues is the abundance of the fibers which are arranged in fiber bundles for the most part, and among which the connective tissue cells *(fibroblasts, fibrocytes)* appear at irregular intervals. The matrix *(tissue fluid)* is a fluid substance which fills the spaces between the fiber bundles and bathes the cells and fibers.

1. CELLS OF CONNECTIVE TISSUE. The following cell types are recognized as being usually present in the fibrous connective tissues: fixed connective tissue cells or fibroblasts, histiocytes or clasmatocytes, mast cells, plasma cells, pigment cells, and wandering cells which are similar to the lymphocytes, eosinophils, and neutrophilic leucocytes found in the blood stream.

a. *Fibroblasts.* The term fibroblast (which is being replaced by the more accurately descriptive term *fibrocyte)* is applied to the cells which are regarded as specifically belonging to the connective tissues. They are large cells, irregularly stellate in form, having a number of processes. They are usually flattened and occupy the narrow spaces between the fiber bundles. Because of their extreme thinness, the colorless and almost nongranular character of their cytoplasm, they can be distinguished only with difficulty in ordinary preparations. Their large, oval nuclei are enclosed by a delicate nuclear membrane and contain a few fine, granular particles of chromatin. When seen in side view, these nuclei are narrow and rodlike. In most preparations only the nuclei of these cells are visible.

Because they do not present a constant outline, fibroblasts are classed as *amorphous cells;* the differences in form being due to a slow protrusion and retraction of their protoplasmic processes in the living

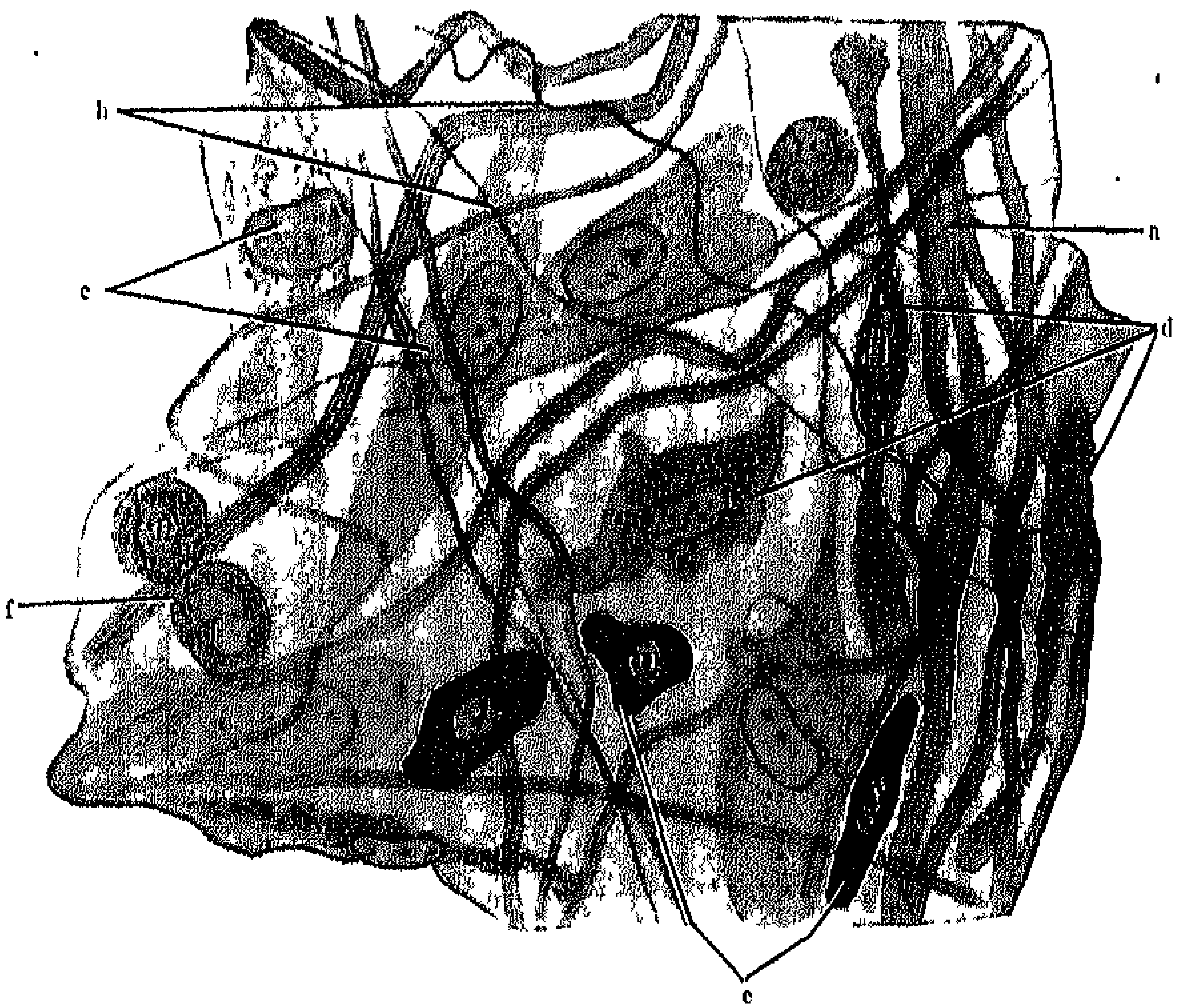


FIG. 22. Fibers and cells in areolar connective tissue. (a) Bundles of collagenous fibers. (b) Elastic fibers. (c) Fibroblasts. (d) Histiocytes. (e) Plasma cells. (f) Eosinophils. (Redrawn from Maximow.)

state. Fibroblasts which are about to undergo mitotic division assume a spherical shape, returning to their usual form after the division has been accomplished.

Functionally, fibroblasts serve as the essential elements in the regeneration of connective tissue. There seems to be little doubt that fibroblasts are related in some way to the formation of the fibers of connective tissues. Although a great deal of attention has been given to the activities of these cells, the exact nature of this relationship is still uncertain. There are two leading theories as to how the formation of the fibers is brought about: first, that the fibroblasts produce a substance which precipitates in the matrix in the form of fibers; second, that the substances of which the fibers are formed are already present in the matrix and are made to precipitate into the form of fibers by a substance which passes into the matrix from the cells.

b. *Histiocytes.* In addition to the fixed cells there are many free or wandering cells which are found in the fluid matrix of the fibrous tissues. Of these the *histiocytes* are the most abundant. They are large, irregularly shaped cells with short protoplasmic processes. In living cells, these processes are slowly protruded and retracted. Histiocytes can be distinguished from fibroblasts by their more deeply staining and more extensively vacuolated cytoplasm and their smaller oval or kidney-shaped nuclei which possess a somewhat coarser nuclear membrane. The nuclei also contain a number of coarser chromatin granules.

When solutions containing finely divided particles are injected into experimental animals, later investigation reveals that a considerable number of these particles are lodged in the cytoplasm of the histiocytes. On the other hand, the cytoplasm of the fibroblasts is found to contain only a few, if any, of the particles. This provides a positive means of identifying these cells. Because of the capacity of the histiocytes for this phagocytic action, they are classed with the group of cells known as *macrophages.*

Cells which do not belong specifically to the connective tissue are known as *wandering cells.* Histiocytes which have become attached to the connective tissue fibers are said to be *resting wandering cells.* When they assume a spherical form and float away in the tissue fluids, they are known as *true wandering cells.*

Histiocytes are stimulated to an intense phagocytic activity by certain conditions, especially those associated with inflammation. They are important elements of the reticulo-endothelial system which will be discussed later.

c. *Mast Cells.* Mast cells are large, round or oval cells which present an irregular outline due to short protoplasmic processes which may project from the cell body. They contain small, round, or oval, pale-staining nuclei which are more or less hidden by the coarse basophilic granules which fill the cytoplasm. Although these cells are capable of slow ameboid movements, they are not known to be phagocytic. They occur in the loose connective tissues and frequently are grouped about blood vessels, especially in regions where fat cells are located; for this reason they are thought, by some investigators, to be active in the formation of fat. Actually, however, their origin or function is not definitely known. Recently it has been suggested that these cells are related to heparin formation. These mast cells of the connective tissues bear a close resemblance to the basophilic leucocytes of the blood.

d. *Plasma Cells.* Plasma cells occur rarely in ordinary connective tissue. They are, however, more abundant in lymphatic tissue (mucous membrane of the alimentary tract) and in the serous membrane of the omenta. Their size is variable and their shape is round or oval. The cytoplasm is homogenous and stains deeply basophilic with the exception of an area near the nucleus which is nearly colorless. The cytoplasm often contains vacuoles. The nuclei, which are eccentrically placed, are small, round and contain triangular masses of chromatin which rest with their bases against the nuclear membrane giving a typical "cart-wheel" appearance. The chromatin masses may also as-same what is known as a "checkerboard" arrangement. These cells are derived from lymphocytes. When these cells begin to degenerate, large droplets of acidophilic material form in the cytoplasm. These droplets are set free with the disintegration of the cell and remain in the connective tissues as *Russell's bodies*. Their function is not known.

e. *Pigment Cells.* These cells are most frequently found in the dense areolar tissue which lies immediately beneath the epidermis of

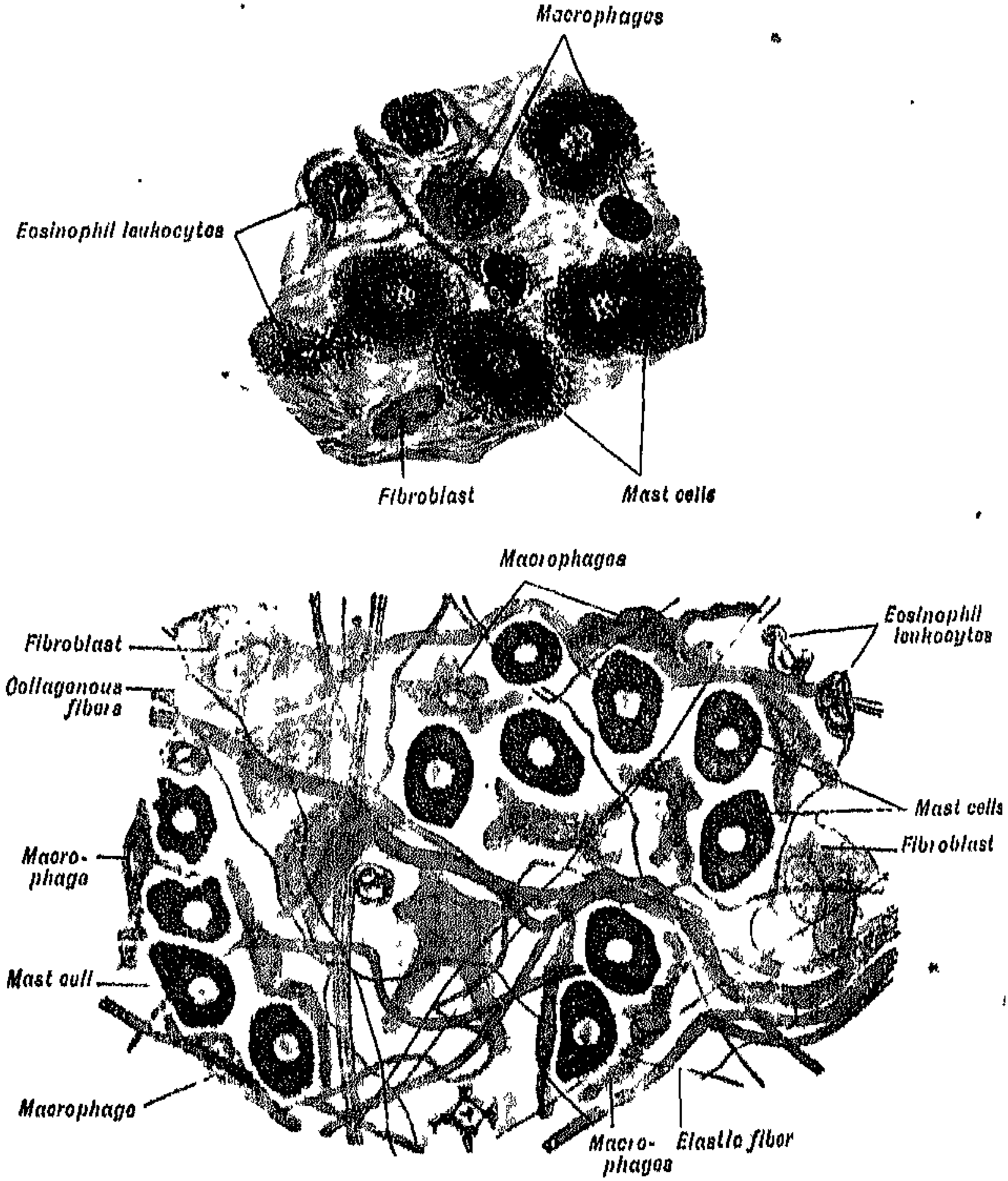


FIG. 23. Two figures from loose connective tissue of the rat. *(Top)* Fixed and stained with hematoxylin-eosin-azure. (600 ×.) *(Bottom)* Stained supravitally with neutral red. (800 ×.) (A.A.M.) (Courtesy, Maximow and Bloom: "A Textbook of Histology," 4th ed., 1942, Philadelphia, W. B. Saunders Co.)

the skin, in the connective tissues associated with parts of the brain, the upper portion of the spinal cord, and in the pigmented portions of the eye. These cells are small and elongated with short, irregular processes. They contain pigment in the form of dark colored granules known as *melanin.* These are highly specialized cells which arise from mesenchymal cells.

f. *Wandering Cells: Lymphocytes, Eosinophils, and Neutrophils.* Cells of the blood and lymph stream frequently wander in among the connective tissue elements. *The lymphocytes* appear as round, deeply staining nuclei surrounded by an almost negligible amount of lightly staining cytoplasm. They occur frequently in the connective tissues where they appear to be associated with plasma cells. With an increase in the amount of their cytoplasm they may assume phagocytic properties. *Eosinophils* are large cells with light staining, bi-lobed nuclei. They are recognized by the coarse, acidophilic staining granules which fill their cytoplasm. The *neutrophils* are also large round cells with pale, irregularly shaped nuclei. Their cytoplasm is filled with fine granules which stain a violet or purple color. They may be actively phagocytic.

2. FIBERS OF CONNECTIVE TISSUES. The fibers of connective tissues are: *white* or *collagenous, yellow* or *elastic,* and *reticular.* In fibrous connective tissues the first two predominate.

a. *White or Collagenous Fibers.* The fibers of white or collagenous connective tissues are extremely fine and delicate. They are bound together by small amounts of cement substance in bundles which vary considerably in size, the fibers lying parallel to one another, and following a wavy course in the bundle. This gives the bundle the appearance of being longitudinally striated. (Some authors refer to the fibers as *fibrillae* and to the fiber bundles as *fibers.*) The fibers do not branch, however, individual fibers, or small bundles of fibers, may leave the fiber bundle and continue independently, or they may join neighboring bundles. This may give the appearance of branching. Collagenous fibers are only slightly elastic; for this reason they form the principal constituent of connective tissue structures which are subjected to a considerable amount of tension, such as capsules, ligaments and tendons. Since they do not refract transmitted light, they appear dark in untreated sections.

When treated with boiling water, collagenous fibers yield a substance known as *collagen;* the substance from which *gelatin* is derived. When dilute acids and alkalies are applied to the fiber bundles, they swell and break up into their constituent fibers. This is probably due to the dissolving of the cement substance by which the fibers are bound together in the bundle. They are digested by the gastric juices, but are not affected by the trypsin-containing pancreatic secretion.

b. *Yellow or Elastic Fibers.* Elastic fibers are larger than collagenous fibers and are not arranged in bundles. The fibers branch freely and anastomose with one another to form irregularly meshed networks. The fibers are highly elastic and when they are pulled apart in teased preparations their broken ends become characteristically curled. Unlike collagenous fibers, they are highly refractive and appear as bright, illuminated lines in unstained tissues. Elastic fibers are easily extended when subjected to strain, but return to their normal state when the tension is released. This is also true of tissues in which elastic fibers are abundant.

Elastic fibers contain a substance known as *elastin.* They are not affected by boiling, nor by the action of dilute acids and alkalies. They are not altered by the action of the gastric juices, but are readily digested by the pancreatic secretion.

c. *Reticular Fibers.* Since reticular fibers do not stain well with ordinary stains, their presence as a part of the general connective tissues of the body has not been recognized. However, with the use of silver stains in studying the tissues and organs of the body more completely, the wide distribution of reticular tissue becomes apparent. Reticular fibers are found closely interwoven around epithelial cells in glandular organs, throughout the substance of the liver and closely applied to the individual muscle cells. In all of these areas the reticular fibers are in intimate relation with collagenous fibers and many of the reticular fibers are seen to be directly continuous with collagenous fibers. In those tissues and organs where the reticular tissue predominates and forms the stroma (lymphoid organs and the tunica propria of the alimentary tract), the cells and fibers are in close relation with one another; the processes of the cells often entwining about the fibers.

Reticular fibers are extremely fine and branch and anastomose to form a delicate network of fibers. They appear to be undeveloped collagenous fibers. They are dissolved by dilute acids and alkalies. When treated with boiling water, these fibers do not yield gelatin, but a substance known as *reticulin.*

3. MATRIX OF CONNECTIVE TISSUE. The matrix of fibrous connective tissue is relatively scanty in amount. It is clear and varies in density from a watery fluid to a jellylike substance which is coagulated by certain agents. This fluid bathes the cells and fibers of the connective tissue and across this thin film of fluid must pass the food and waste products of the cells. Within it move the wandering cells and the histiocytes of connective tissue that protect the body against harmful foreign substances.

Since the relative proportion of these different constituents varies considerably, and in some instances the arrangement of fibers likewise differs, it is customary to subdivide further the fibrous connective tis-

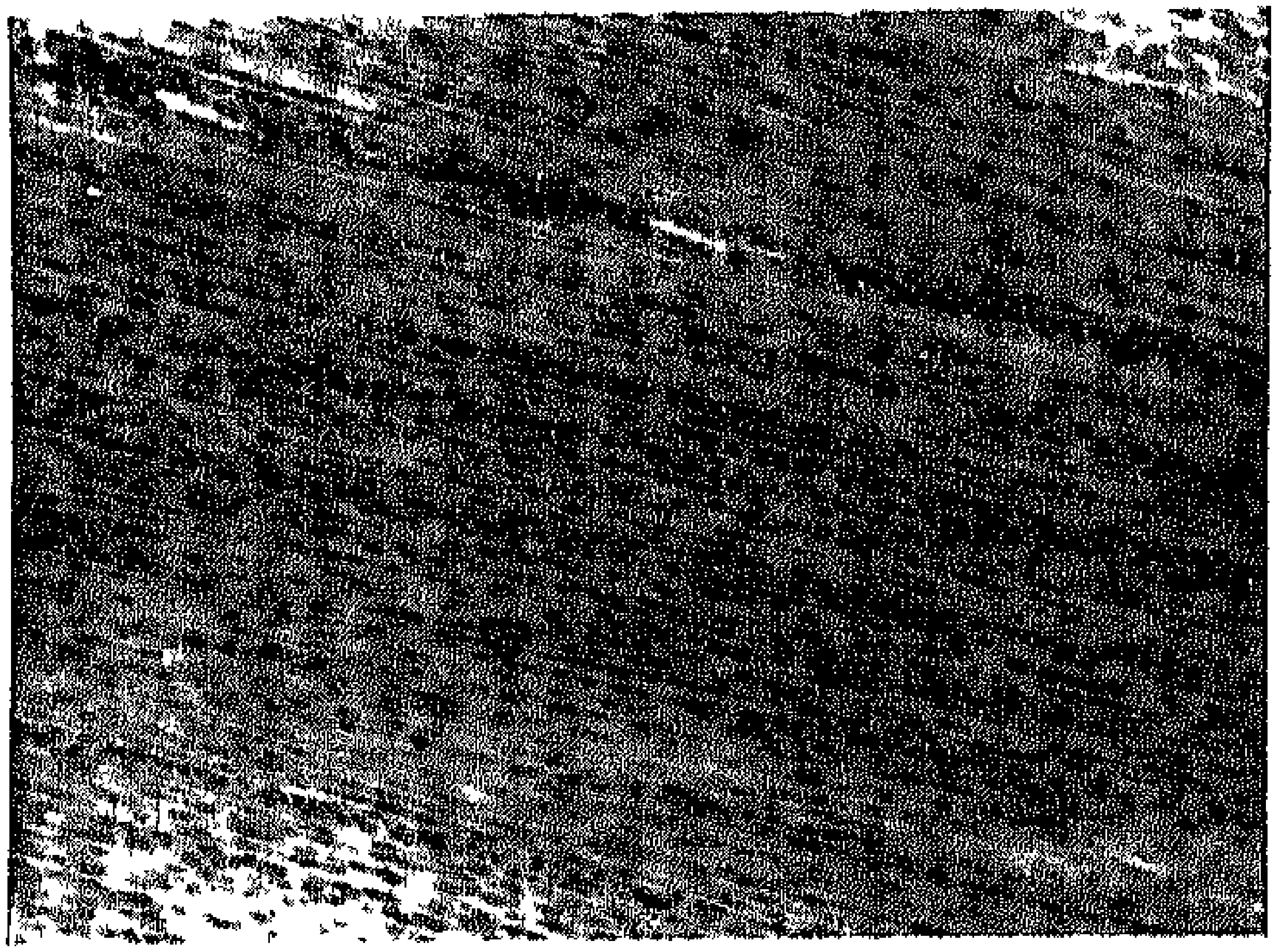
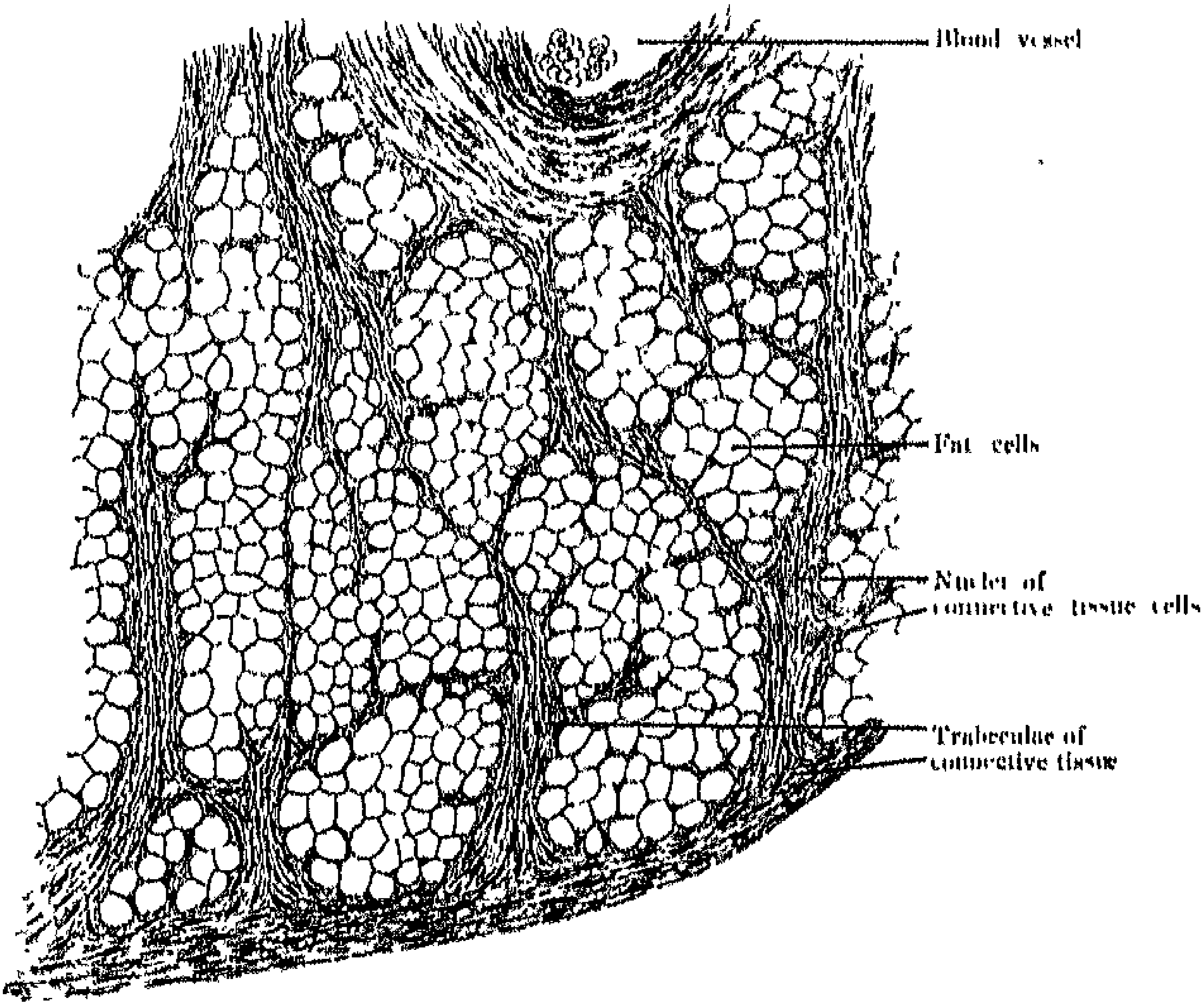


FIG. 21. Elastic connective tissue (ligamentum nuchae) longitudinal section. The nuclei of dense elastic tissue are more numerous and closer together than the nuclei of the tendon. In dense elastic tissue the nuclei are shorter and more oval than the nuclei of tendon. Photomicrograph.


Blood vessel
Fat cells
Nuclei of connective tissue cells
Trabeculae of connective tissue

sues for classification and study into: *areolar* (loose and dense), *dense fibrous connective tissue* (tendon), and *elastic connective tissue.*

AREOLAR (FIBRO-ELASTIC) CONNECTIVE TISSUE. Areolar tissue is the most widely distributed tissue in the body. It consists of cells, a fluid or semifluid matrix and both collagenous and elastic fibers which interlace in all directions. Spaces *(areolae)* of varying size occur between the fiber bundles.

DENSE AREOLAR. The fiber bundles are closely interwoven, as in the tissue which underlies the epidermis of the skin.

LOOSE AREOLAR. The fiber bundles are more loosely arranged to form a soft, yielding tissue. It is found beneath the skin, which it connects with the underlying structures *(tela subcutanea).* It surrounds and supports the blood vessels and nerves; it also surrounds the various organs and aids in attaching them to adjacent structures. In the form of *septa,* it provides the pathways by which the blood vessels and nerves pass to their terminal distributions in the organs.

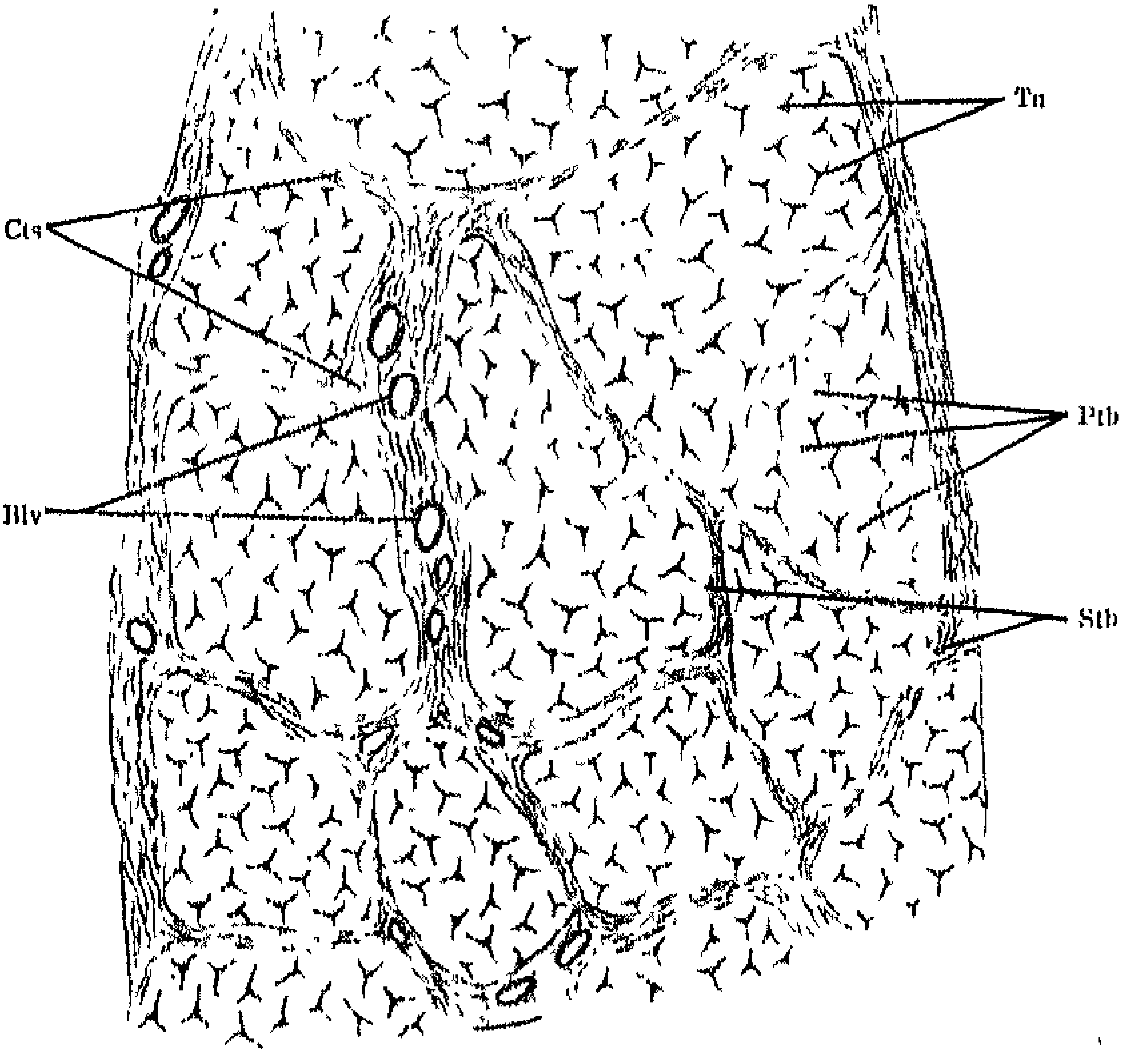


FIG. 26. Cross section of tendon bundles more highly magnified. Drawn from a section. (Tn) Nuclei of tendon cells (winded nuclei). (Ptb) Primary tendon bundles. (Stb) Secondary tendon bundles. (Cts) Septa of connective tissue separating the secondary bundles. (Blv) Blood vessels following the septa.

DENSE FIBROUS CONNECTIVE TISSUE (TENDON). This tissue is characterized by closely packed fibers, predominately collagenous, with elastic fibers being either absent entirely or present in very small quantity, and by having great tensile strength with practically no stretch. This tissue occurs in capsules, ligaments, aponeuroses and tendons. The tendon provides the best example for study.

In tendons the fiber bundles consist of numerous fibers bound together by a cementing substance *(tendomucoid)*. The fiber bundles lie parallel to one another, the fibers pursuing a wavy course in the bundles. The tendon cells lie between the fiber bundles, by which they are compressed into flattened, protoplasmic plates which have a tendency to fold around the bundles. When the tendon is seen in cross section, the cells appear to have winglike processes which extend between the fiber bundles.

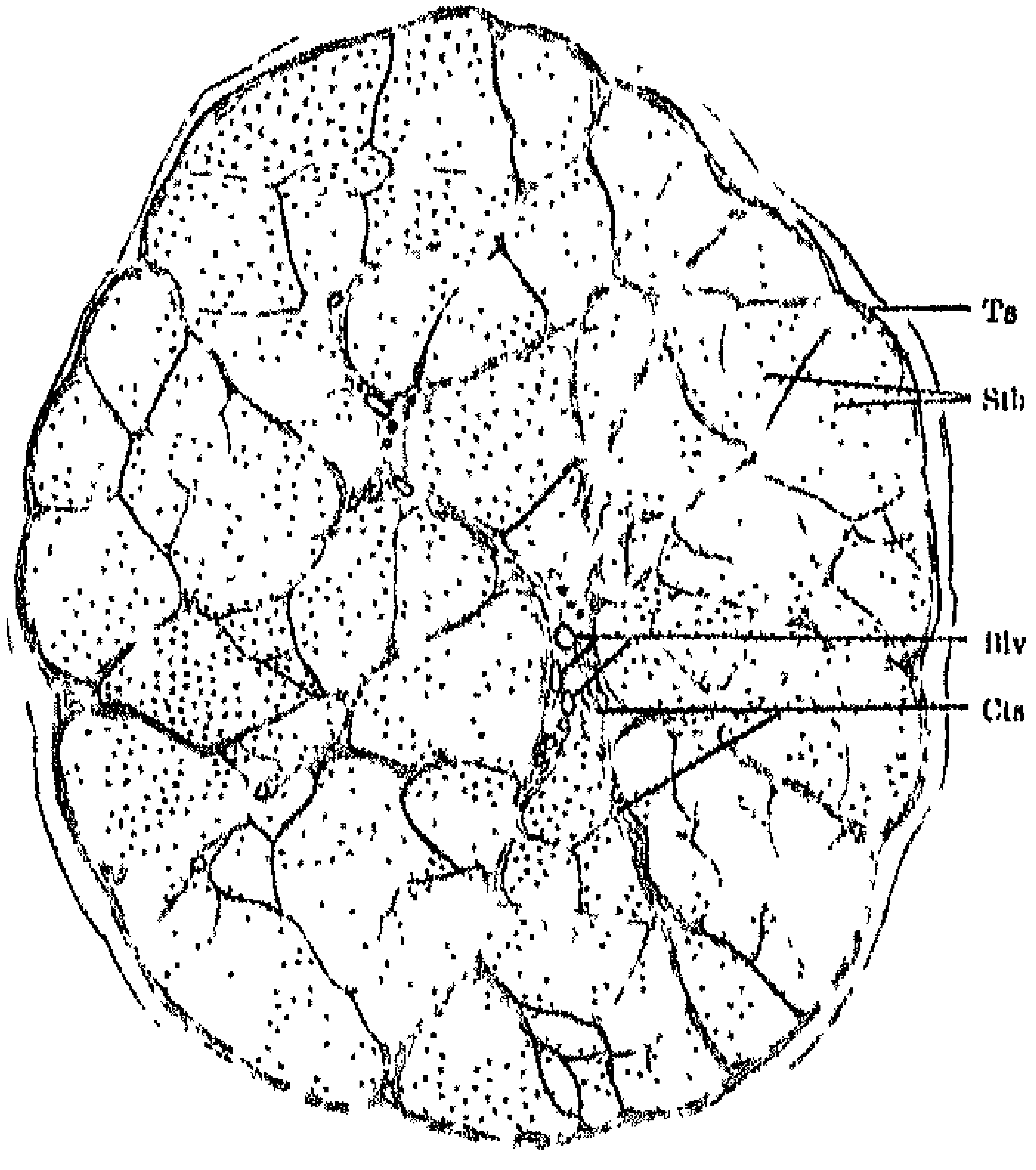


FIG. 27. Cross section of a tendon. (Ts) Tendon sheath (external peritendineum). (Stb) Secondary tendon bundles (Blv) Blood vessels. (Cts) Connective tissue septa (internal peritendineum) surrounding the tendon bundles. (After Sobotta.)

When the cross section of a tendon is examined, it is seen to be enclosed by an outer covering of closely interwoven collagenous and elastic fibers *(external peritendineum)*. This layer of fibrous tissue forms the tendon sheath (*vagina fibrosa*). In some cases a cavity is formed by the splitting of the sheath into outer and inner layers, the space between these layers being filled with a fluid containing a mucoid substance. This is known as a *mucous sheath (vagina mucosa)* and it provides for free movement of the tendon within its sheath. Connective tissue septa extend from the external peritendineum into the tendon *(internal peritendineum)*, and divides it into secondary and tertiary bundles.

The fibers of the connective tissue sheaths which surround the muscles *(fascias)*, and which form capsules, ligaments and aponeuroses, are arranged in much the same way as in the tendons, with the exception that, while the fibers of a single layer are parallel, the layers frequently cross one another at right angles. This is especially the case in aponeuroses. Elastic fibers are practically absent from tendons, but may be present in other forms of dense fibrous tissue.

ELASTIC TISSUE. Elastic fibers are seldom found forming a pure tissue, but in a number of places in the body, elastic fibers predominate. Examples are the wall of the aorta and smaller arteries where the elastic fibers form the so-called fenestrated membrane of the wall.

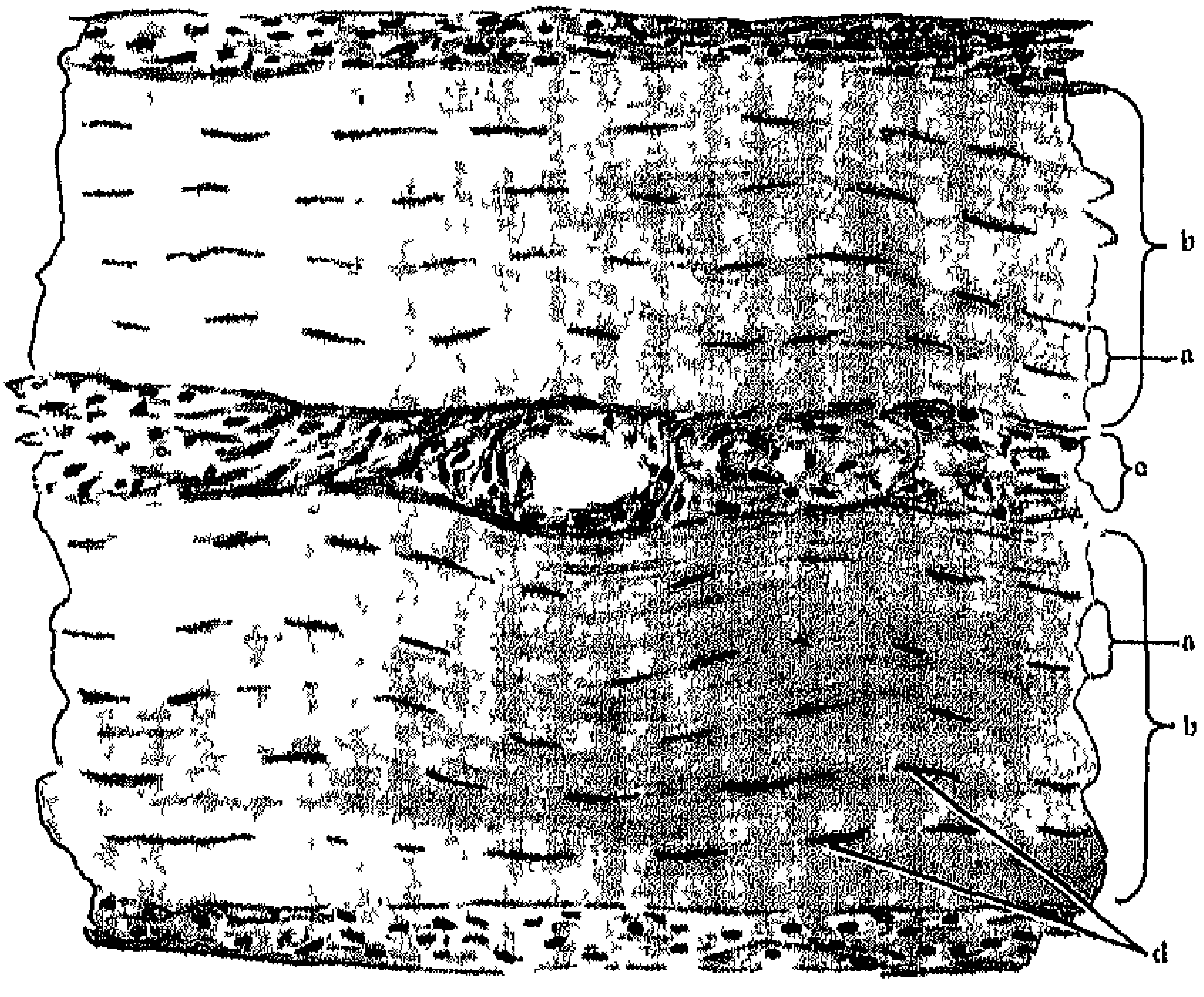


FIG. 28. Longitudinal section of tendon. (a) Primary bundles or bundles of tendon fibers. (b) Secondary bundles or tendon fasciculi. (c) Interfascicular connective tissue. (d) Nuclei of tendon cells.

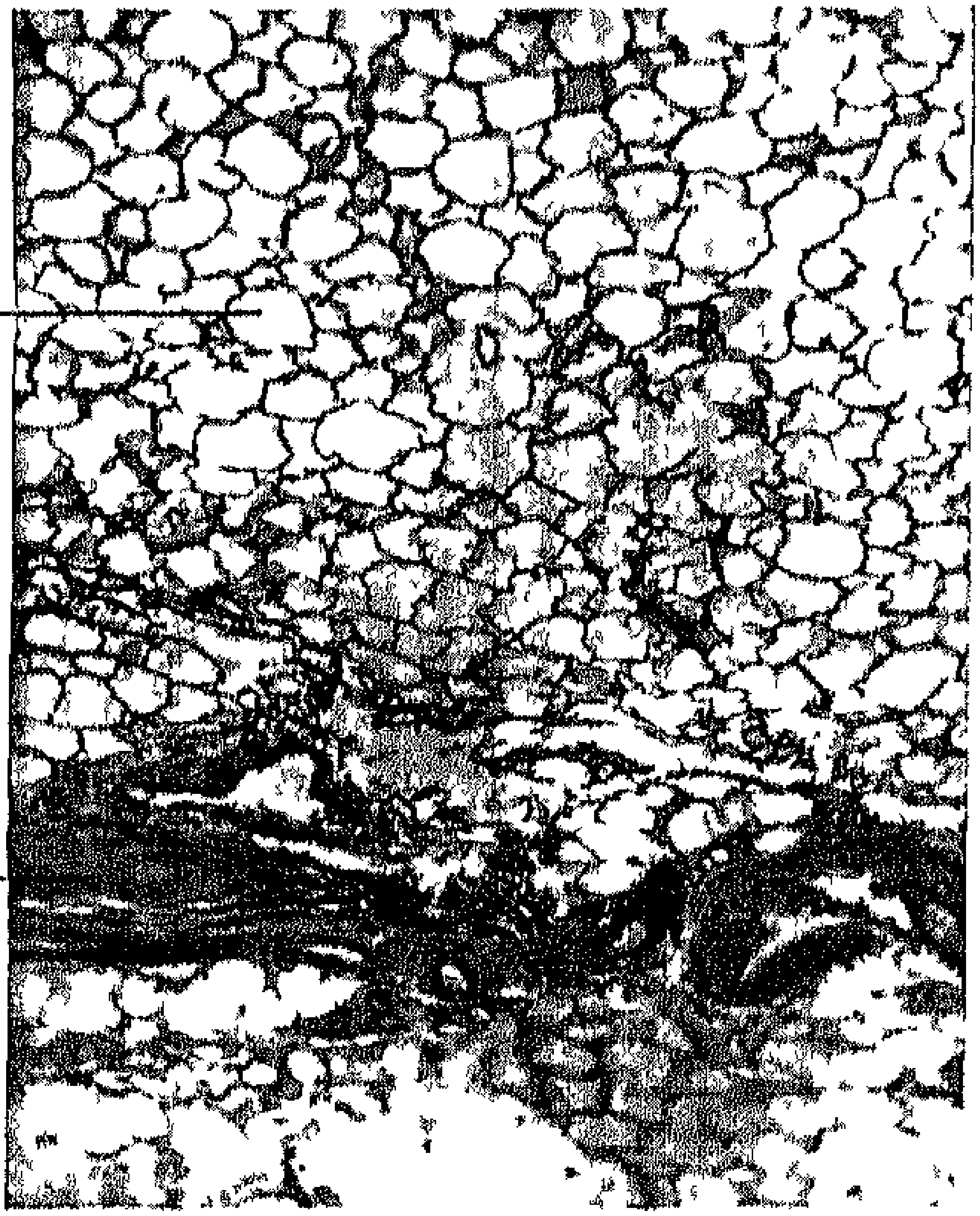


FIG. 29. Adipose tissue with connective tissue trabecula. Stained with silver nitrate. Photomicrograph.

They are present in quantity also in the trachea and bronchi. In general, ligaments show a predominance of elastic fibers. The ligamentum nuchae of the ox is almost pure elastic tissue and forms an excellent material for study.

The fibers in this ligament are in parallel arrangement and are quite coarse. Loose connective tissue surrounds the entire ligament and sends septa down to divide it into relatively large segments. This connective tissue further divides to enclose even the individual elastic fibers in delicate sheaths.

ADIPOSE TISSUE

Any of the cells of connective tissue may assume the special function of storing fat. These fat cells may exist singly or in mass, but when they occur in large numbers, it is customary to refer to them as adipose tissue. Adipose tissue occurs in connection with loose areolar tissue. It forms a layer in the subcutaneous connective tissue of the skin, the thickness depending on the nutritive state of the indi-

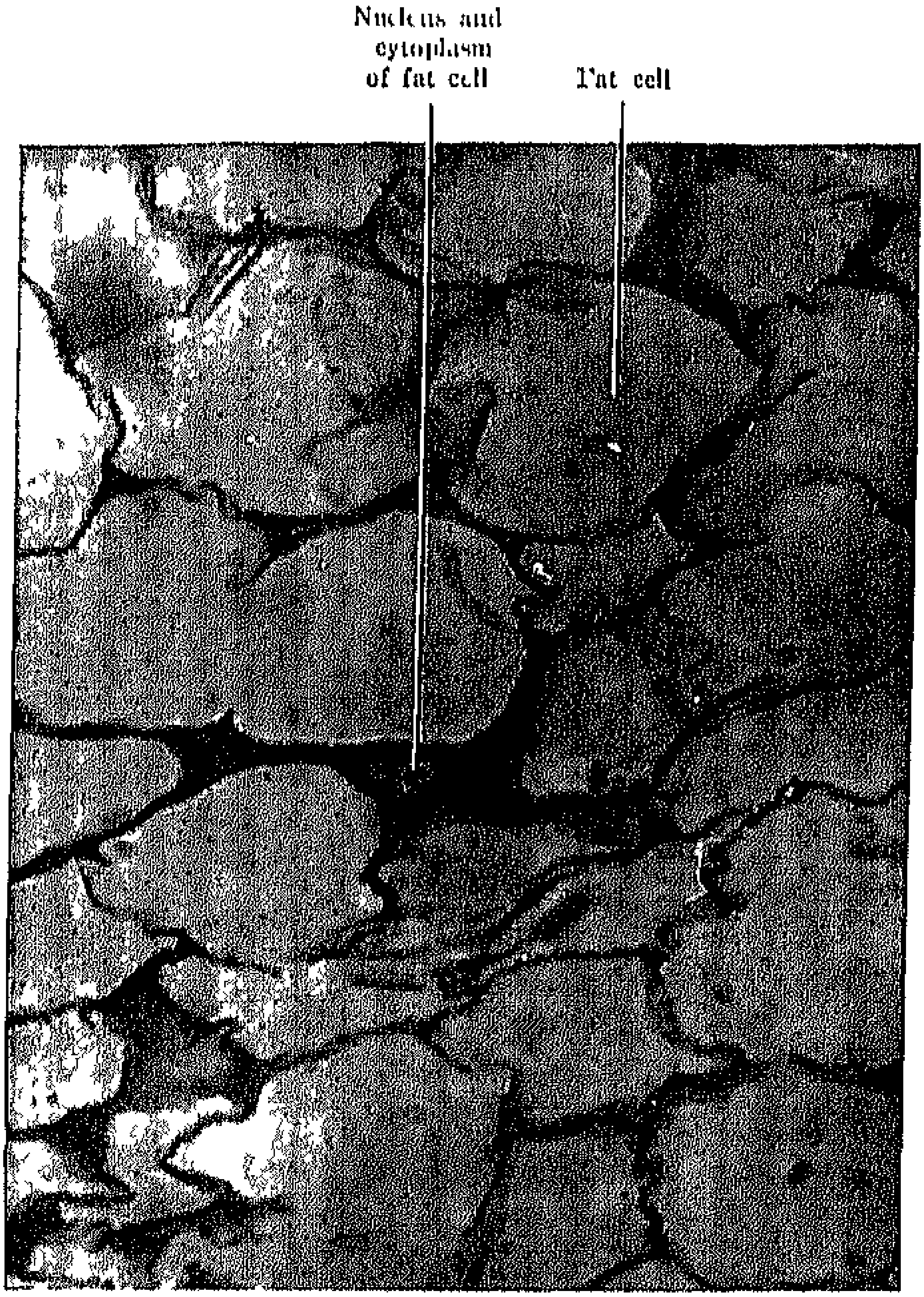


FIG. 30. Fat cells under high magnification. One cell shows the nucleus and small amount of cytoplasm crowded to one side of the cell. The fat has been dissolved out leaving the clear empty spaces. Stained with silver nitrate. Photomicrograph.

vidual. This tissue also forms a cushion around the kidney, in the furrows of the heart, in the bone marrow, and in the mesenteries.

Unlike the other fibrous connective tissues with which it is so closely related, the predominant element of adipose tissue is cells, not fibers. Each individual cell is a large, globular body, the form of which is dependent on the amount of fat it contains and the pressure of adjacent tissues. The globule of fat is surrounded by a thin pellicle of cytoplasm. The nucleus, which has been pressed to one side of the cell, is surrounded by a small amount of granular cytoplasm. This gives the fat cell its characteristic "signet-ring" appearance. The nuclei are pale, oval and flattened in surface view. When seen in side view, they appear as elongated structures which are difficult to distinguish from the nuclei of the closely associated connective tissue cells. In sectioned material, the fat is usually dissolved by the reagents used in preparing the tissue and the cells appear as clear spaces outlined by a thin membrane.

In adipose tissue the fat cells are closely crowded together in lobular masses, the lobules being separated by trabeculae of fibrous connective tissue. Delicate fibers extend from the trabeculae between the cells and bind them together. Each lobule is supplied by a blood vessel about which the fat cells are massed, its branches breaking up into small capillaries which lie in close relation to the cells.

Adipose tissues, especially in the axillary and inguinal regions, around the kidney, and in certain other locations, are differentiated in the embryo and are present at birth. These tissues are believed to represent definite fat organs. In other localities, especially in the connective tissues of the skin, the muscles, and the mesenteries, fibroblasts appear to be transformed into fat cells by the accumulation of fat droplets in their cytoplasm. The origin of these fat droplets is not known. On losing their fat, these cells revert to their original fibroblastic condition.

THE RETICULO-ENDOTHELIAL SYSTEM

The term reticulo-endothelial system is a poorly chosen term since the name fails to indicate or designate what is actually meant. In the usual sense of the word it is not a system, and none of the cells in this system are truly endothelium.

This "system" actually consists of all the phagocytic cells of the body, excluding only the leucocytes. They are distinguished from other cells of the body by their capacity to ingest *(phagocytize)* particular matter of any kind which may be present in the blood, lymph or tissue fluids. The cells of this system are scattered throughout the tissues and organs of the body. They may differ from each other morphologically and in their location, but they all react similarly. Their origin is unknown.

The only positive means of identification of the cells of this "system" is to inject into an experimental animal a weak solution of any of the vital stains, such as lithium carmine, trypan blue, or colloidal carbon solution. After such staining, the dye or carbon particles will be found in the cytoplasm of these cells, which may be briefly listed as follows:

1. Histiocytes—in connective tissue and in the blood stream.
2. Kupffer cells—in the liver sinusoids.
3. Reticular cells—of sinuses of lymph nodes, and in lymphoid tissue, bone marrow, lining sinuses of the adrenal gland and pituitary gland.

4. Microglia—of the nervous system.
5. "Dust cells"—of the lungs.

The cells of this system play an extremely important part in the defense reactions of the body and in its general metabolism. In defense reactions their role is the destruction of invading bacteria or removal of foreign materials. They may be important in immunity by their production of antibodies. In the general metabolism of the body these cells dispose of disintegrating cellular material, and some believe they also aid in fat transportation.

5

Connective Tissues (Cartilage)

Like other connective tissues cartilage consists of cells, fibers and a matrix. The matrix, however, has become modified and has acquired a degree of firmness which enables it to resist tension and pressure to a certain extent. With the exception of the flat bones of the face and cranium and probably the clavicle, the entire skeletal framework in man is first laid down in cartilage. It is found in the adult human body as a covering for the articular surfaces of bones and forming the framework of the larynx, trachea and bronchi.

The three forms of cartilage which occur in the body, classified according to the fibers present in the matrix, are: *hyaline*, *fibrous*, and *elastic*.

HYALINE CARTILAGE

Hyaline cartilage is formed from the cells of the original mesenchyme. These cells become closely aggregated and with the disappearance of the intercellular spaces assume the appearance of a syncytium. Changes now take place in the tissue fluid between the cells to form the matrix. This ground substance consists chemically of chondromucoid, chondroitin-sulfuric acid and albumoid. It also contains both collagenous and elastic fibers which are formed at the same time as the matrix. This matrix material increases in amount and its character is such that it hides the presence of the fibers embedded in it, so that it appears as a homogeneous ground substance. With this increase, moreover, the cells are pushed farther and farther apart. The fibers of the connective tissue immediately adjacent to the surface of the cartilage assume a regular, usually longitudinal arrangement and form an investing sheath, the *perichondrium*. All forms of hyaline cartilage are enveloped by perichondrium, except those which are interposed between the bones in joints *(articular cartilage)*.

Hyaline cartilage receives its name from its clear, translucent, whitish appearance. When found in certain cuts of beef it is known as "gristle." Its color in the fresh condition is white with a slight bluish tinge. It is the most widely distributed of all forms of cartilage. In the embryo it is present in structures which represent nearly the entire skeleton, and will be replaced by bone in later stages of development. In this case the embryonic skeleton is said to be *preformed in cartilage*. It forms the cartilages which support the alae, or wings of the nose, the greater part of the cartilages of the larynx, the cartilages which form the rings of the trachea and bronchi, the cartilages which attach the ribs to the sternum, the xiphoid process, and the articular cartilages which cover the opposing surfaces of bones in joints.

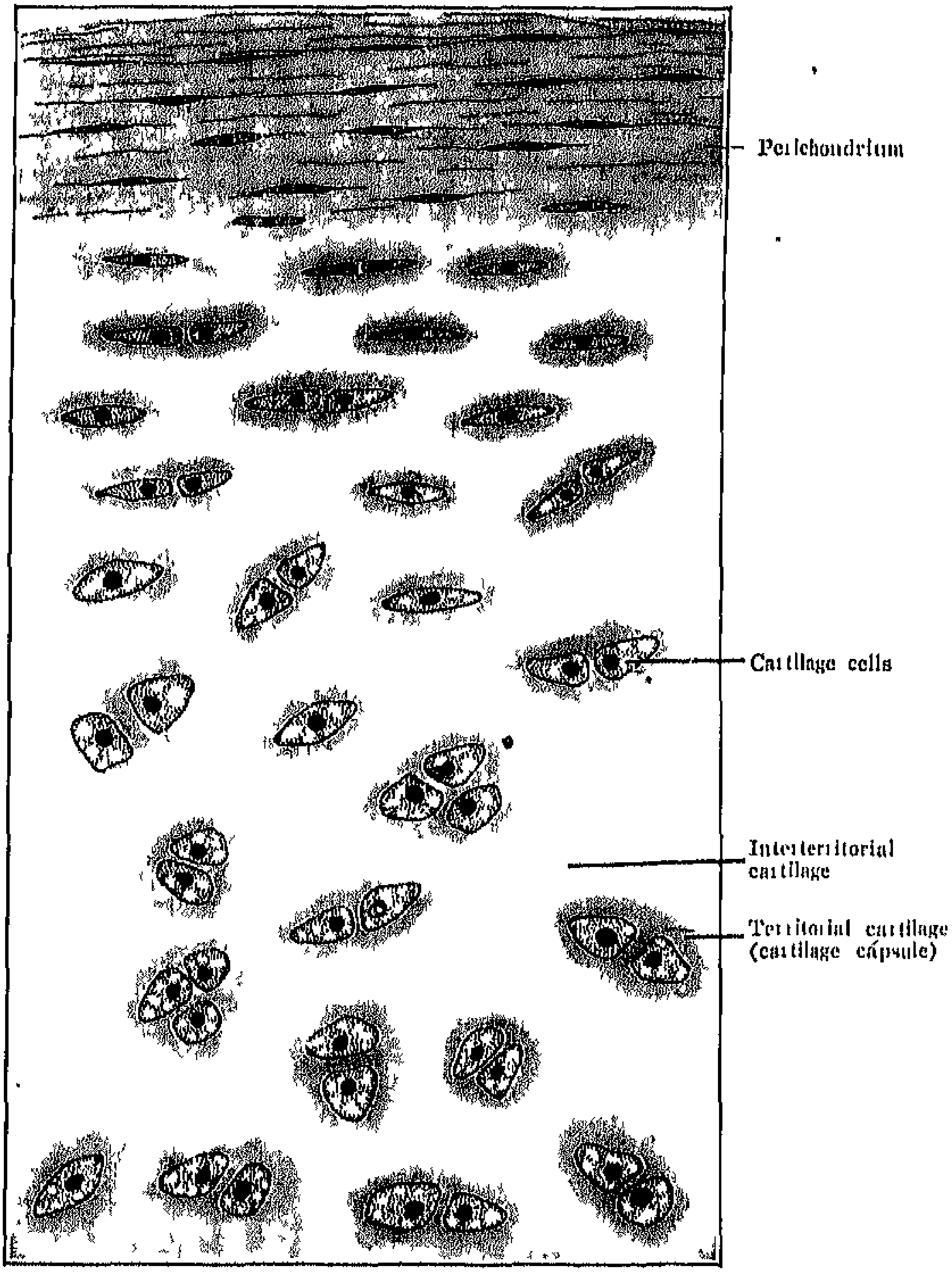

Perichondrium
Cartilage cells
Interterritorial cartilage
Territorial cartilage (cartilage capsule)

FIG. 81. Hyaline cartilage from costal cartilage of an adult.

5

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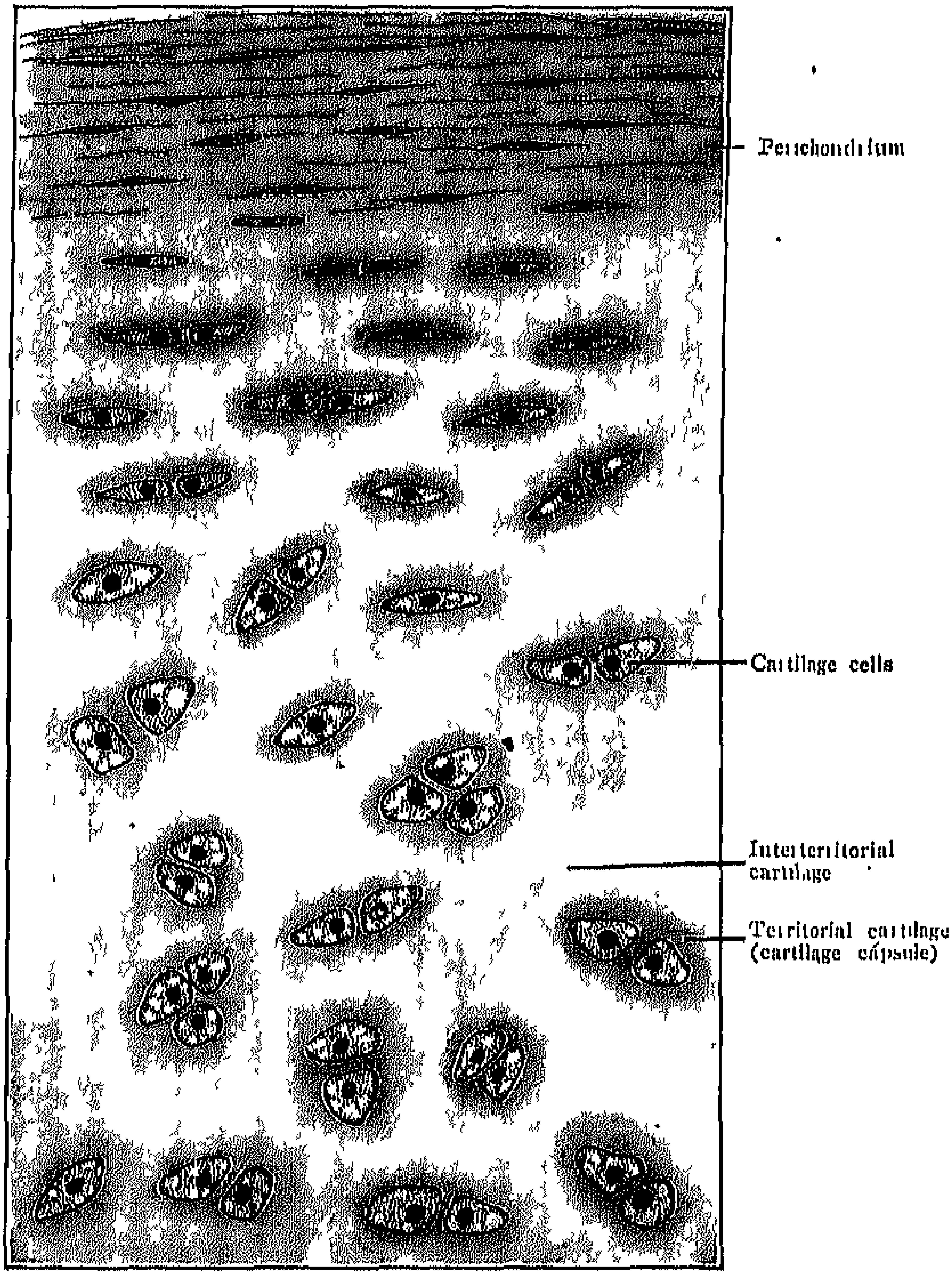

Perichondrium
Cartilage cells
Interterritorial cartilage
Territorial cartilage (cartilage capsule)

FIG. 81. Hyaline cartilage from costal cartilage of an adult.

In mature cartilage, the matrix is more or less homogeneous, and the cells are located in spaces called *lacunae*. These cells vary in shape from flattened ovals to round, depending on their location in the cartilage, and they fill the lacunae in which they lie. The cartilage cells which are located just below the perichondrium are flattened, their long axes being parallel to the surface of the cartilage. They gradually assume a more rounded shape in the deeper layers. The nuclei are large, centrally placed and contain one or more nucleoli. The cytoplasm of the cells contains fine granules and droplets of fat and glycogen. In preparing tissue for sectioning, the fat has been dissolved from the cells, leaving them vacuolated and shrunken. In the embryonic state the cells have processes, but these disappear in adult cartilage, before interstitial growth has developed. In the older portions of the cartilage in adults, when mitosis of cells occurs, the density of the matrix prevents the cells from separating after they have divided. Consequently several cells will be found occupying the same lacuna or separated only by a thin partition of cartilage. In mature cartilage the area immediately surrounding the lacunae in which the cartilage cells are located is called *territorial cartilage* and represents the newly formed matrix. The territorial cartilage stains more deeply basophilically due to concentration of chondromucoid. The older cartilage between the territorial cartilage contains albumoid and is known as *interterritorial cartilage*. For this reason the staining reactions of the two areas are not the same. The territorial areas which surround the lacunae, which are commonly known as the *cartilage capsules*, stain blue (basophilic) with haematoxylin and eosin. This reaction may be modified in sections in which the chondromucoid and chondroitin-sulfuric acid have been removed by reagents employed in preparing the tissue. The interterritorial cartilage between the cartilage capsules is much firmer owing to its increased density. Its normal staining reaction tends to be acidophilic (due to the albumoid present) and stains red, and it appears much lighter than the territorial areas. The staining reaction of the older cartilage in the interterritorial areas may become intensely basophilic (blue staining) due to the precipitation of calcium salts in the matrix *(calcification)*. The depth of color will vary with the amount of calcium present.

Chondromucoid, which with chondroitin-sulfuric acid and albumoid forms the matrix of cartilage, is a mucinogenous substance which stains blue with basic dyes. Chemically it is closely related to the proteins. It is insoluble in water but soluble in very dilute alkalies. It contains no phosphorus, yet has many reactions of the nucleoproteins. Unlike collagen and gelatin it is not precipitated by tannic acid.

Chondroitin-sulfuric acid is found for the most part in the terri-

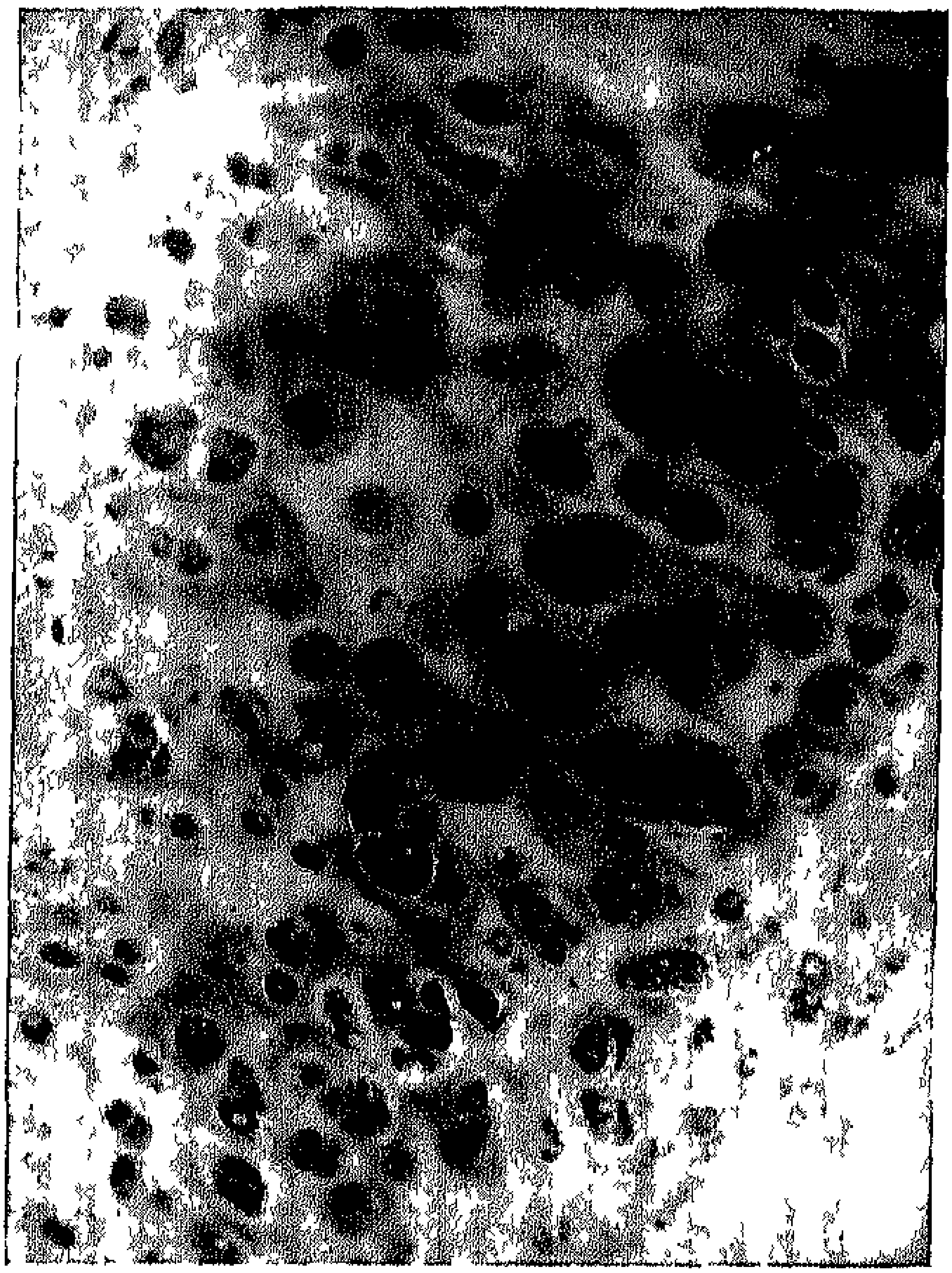


FIG. 32. Hyaline cartilage from the trachea. The older cells through the center of the section are arranged in groups (As the cells approach the periphery of the cartilage they are single and somewhat flattened.) Photomicrograph.

torial cartilage where it is associated with chondromucoid. These two substances are responsible for cartilage having basophilic properties. It is water soluble, which explains why cartilage loses its basophilic character when soaked for a long time in water.

Albumoid is related to both elastin and keratin. It differs from elastin in containing more sulfur, and from keratin in being digested by the gastric secretions. It is present in adult and old cartilage. The amount of chondromucoid decreases, and that of albumoid increases as cartilage grows older.

In addition to the above-named substances, cartilage also contains collagen, which is reducible to gelatin, and a number of inorganic salts, among which sodium chloride occupies an important place.

The growth of cartilage takes place in two ways: first, by *apposition* or addition of new cartilage at the surface of the cartilage plate; second,

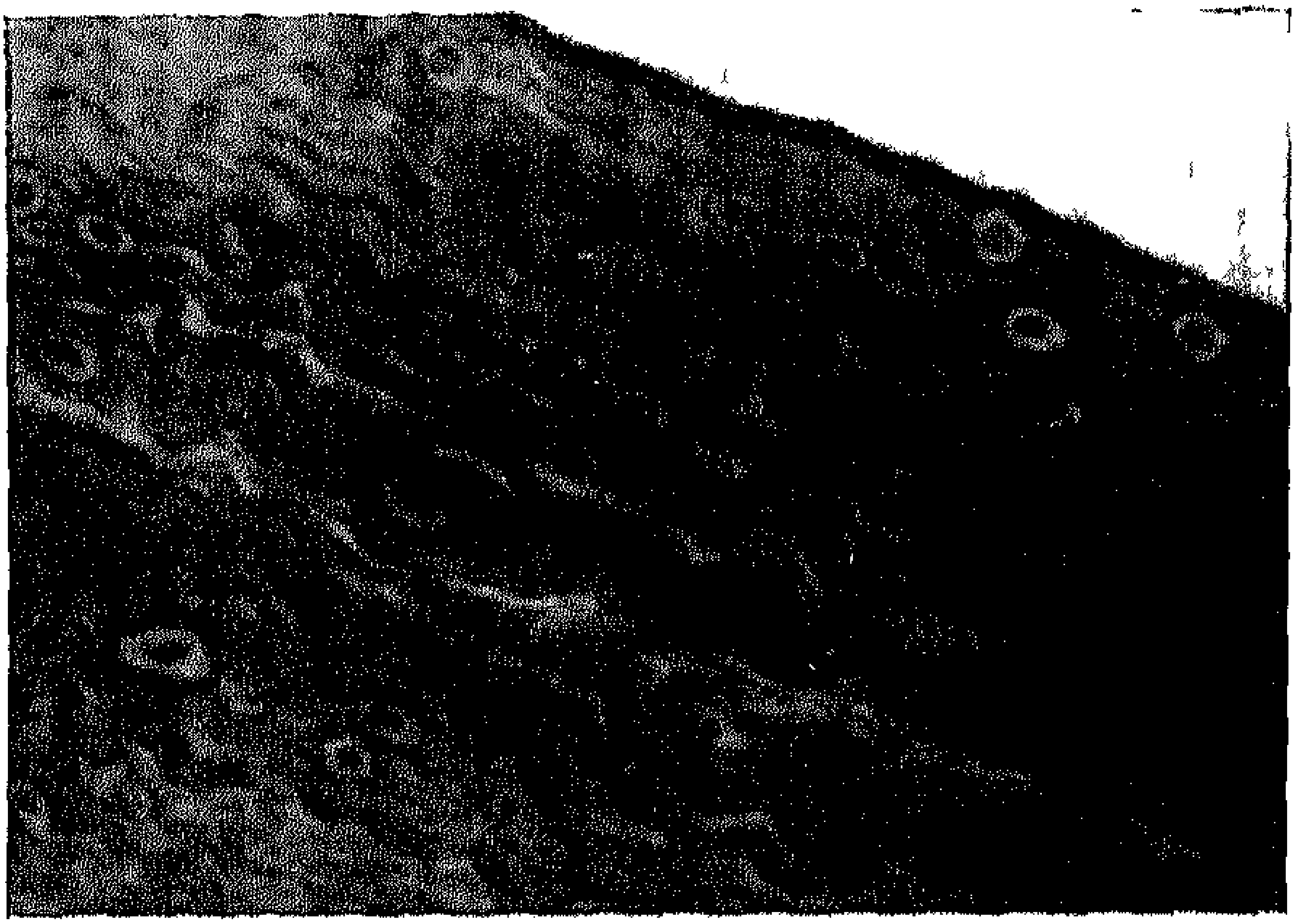


FIG. 39. Fibrous cartilage from the intervertebral disc of a child. The cartilage cells which lie between the bundles of wavy collagenous fibers show a linear arrangement. Photomicrograph.

the density of the matrix increases with age in the cartilage is also shown by the fact that it has a bluish tinge when stained with haematoxylin and eosin, instead of being clearly transparent as in the earlier condition.

Fibrous cartilage is to be found in the intervertebral disc; it is the cartilage which borders the glenoid fossa of the shoulder and the acetabulum of the hip, and is found in the interarticular joints of the sternum and clavicle, and of the clavicle and acromion process, the articulation of the jaw, and the cartilage of the symphysis pubis.

ELASTIC CARTILAGE

Elastic cartilage is similar to hyaline cartilage except that it has numerous elastic fibers in its matrix in addition to many fine collagenous fibers. The cells occupy large, rounded lacunae, and are very seldom found in groups. The matrix is yellowish in color in the fresh condition, owing to the presence of the elastic fibers. The cartilage capsules *(territorial cartilage)* which surround the lacunae are much lighter in color than the remaining portions of the cartilage.

The elastic fibers form a more or less dense network in the deeper portions of the matrix. They are less abundant at the periphery of the cartilage, from which they may be traced into the surrounding perichondrium. Some areas of the matrix may be entirely free from elastic

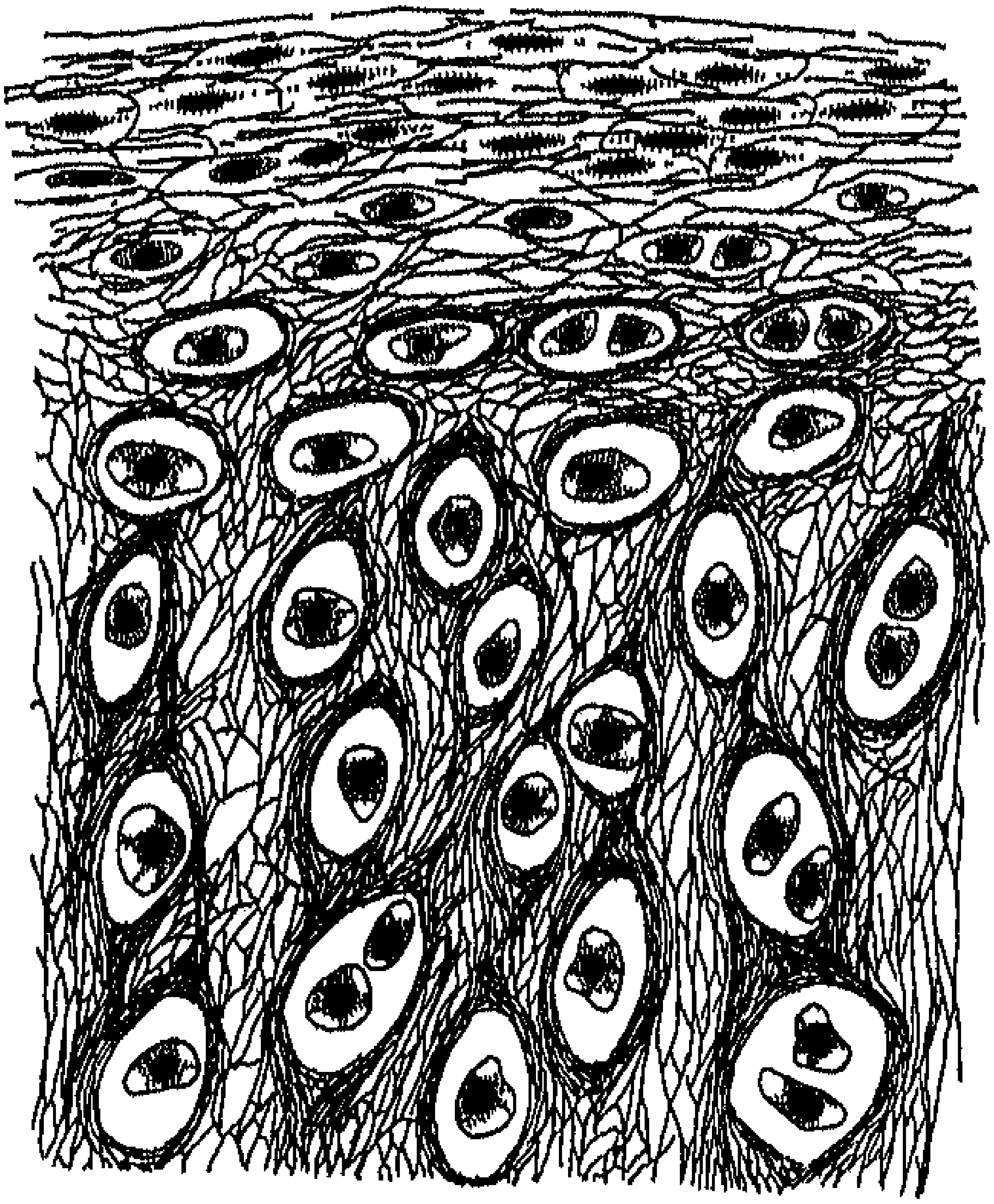


FIG. 91. Elastic cartilage. From the cartilaginous plate of the ear. Drawn from a section prepared by Verhoeff's elastic tissue stain.

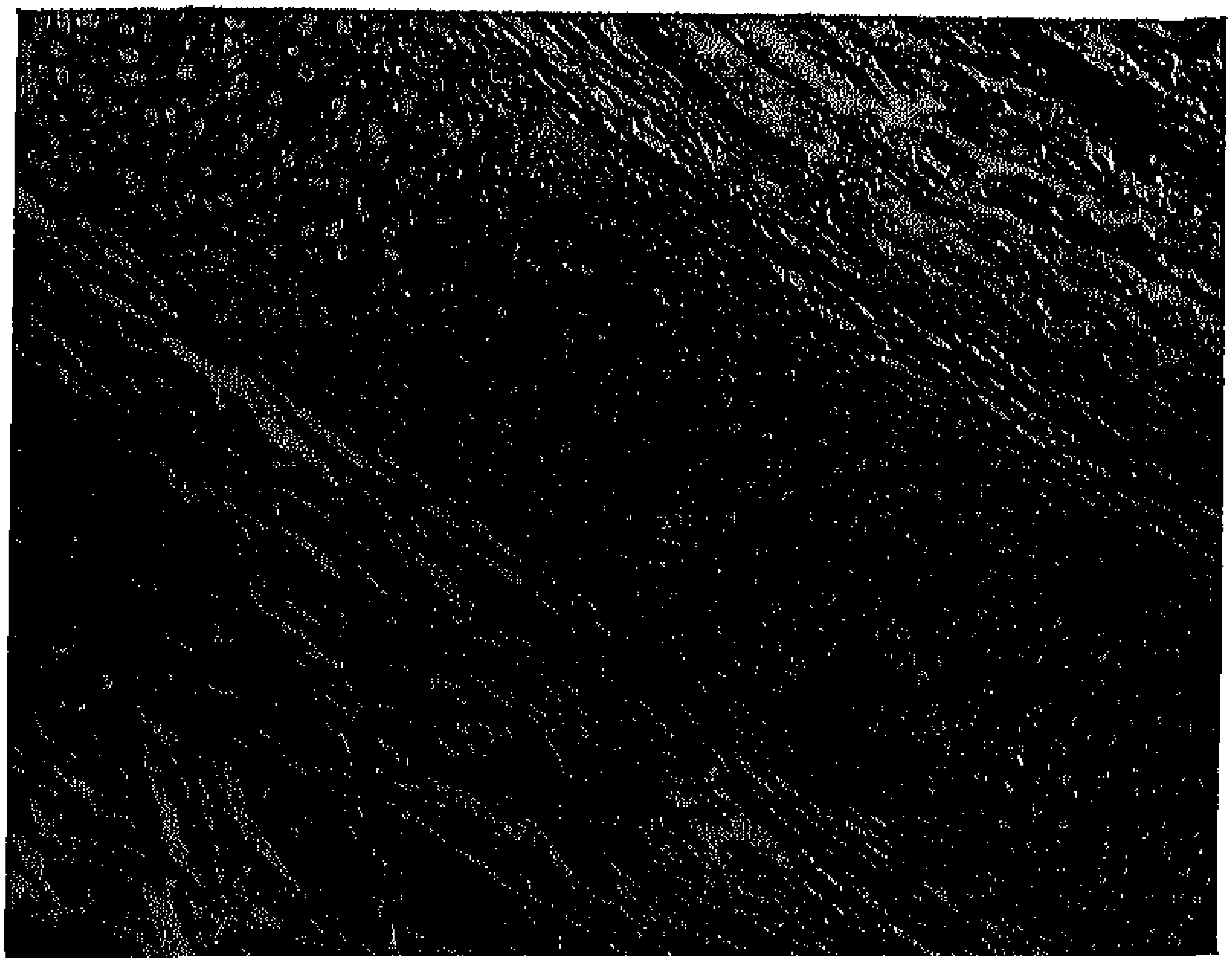


FIG. 36. Elastic cartilage from the ear showing an area of Fig. 35 under high power. Verhoeff's elastic tissue stain. Photomicrograph.

fibers, in which case it has the appearance of, and is probably identical with, hyaline cartilage.

Elastic fibers are not present in the cartilage capsules, but appear only in the interterritorial areas. This supports the belief that the elastic fibers arise in the matrix, the manner in which the cells influence their production being unknown.

The belief that elastic cartilage is a typical hyaline cartilage, differing only in the presence of elastic fibers, is borne out by the conditions existing in the arytenoid cartilages of the larynx. The bodies of these cartilages consist of the usual type of hyaline cartilage, then elastic fibers begin to appear as the cartilage extends into the vocal processes, and the processes themselves become definitely elastic in character.

Elastic cartilage appears in the cartilaginous plate that supports the pinna of the ear, in the cartilage of the Eustachian tube, in the corniculate and cuneiform cartilages, and the vocal processes of the arytenoid cartilages of the larynx.

6

Connective Tissues (Bone)

STRUCTURE OF BONE

Bone, although a connective tissue, is one of the hardest tissues of the body. This is due to the character of the matrix, which has become modified through impregnation with certain inorganic materials. The most important of these salts are *calcium phosphate,* which is the most abundant, *calcium carbonate, calcium fluoride,* and *magnesium chloride;* the last two named being present only in small quantities.

Being a connective tissue, bone consists of cells *(osteocytes)* and fibers which are embedded in an organic matrix containing mucoid *(osteomucoid)* and albuminous *(osteoalbumoid)* substances. These are combined to form a material known as *ostein* which, in appearance, closely resembles some forms of cartilage.

The organic and inorganic constituents are combined in a way which is characteristic of bone, and which give it hardness and strength. The intimate nature of this combination can be shown by two experiments. If one of the long bones is treated with an acid solution, the inorganic salts are dissolved *(decalcification),* the organic constituents alone remain. When this has been completed, the bone retains its original size, shape and characteristic markings, although it can be readily bent and twisted. On the other hand, when the organic material has been removed by exposing the bone to intense heat *(calcination),* the size, form and markings of the bone remain as before, but it has a chalky appearance and texture, and shows a marked tendency to crumble.

Bone serves several important functions in the body. (1) It forms the skeleton or framework. (2) It affords attachment for the skeletal muscles and by their contraction the bones are converted into a series of levers which make movement of the body possible. (3) In some regions the bones are converted into bony cages which hold and protect the more delicate and vital organs of the body. (4) Bone is one of the important hemopoietic organs of the body. The red marrow of long bones in the fetus and in children, and red marrow of vertebrae, ribs, sternum, epiphyses of long bones, and cranial bones in adults, is the site for the formation of most of the blood cells.

If a longitudinally split long bone is examined grossly, it is at once evident that two types of bony tissue are present. (1) A hard, outer investing layer of *compact bone*. (2) A loose, spongy type of tissue

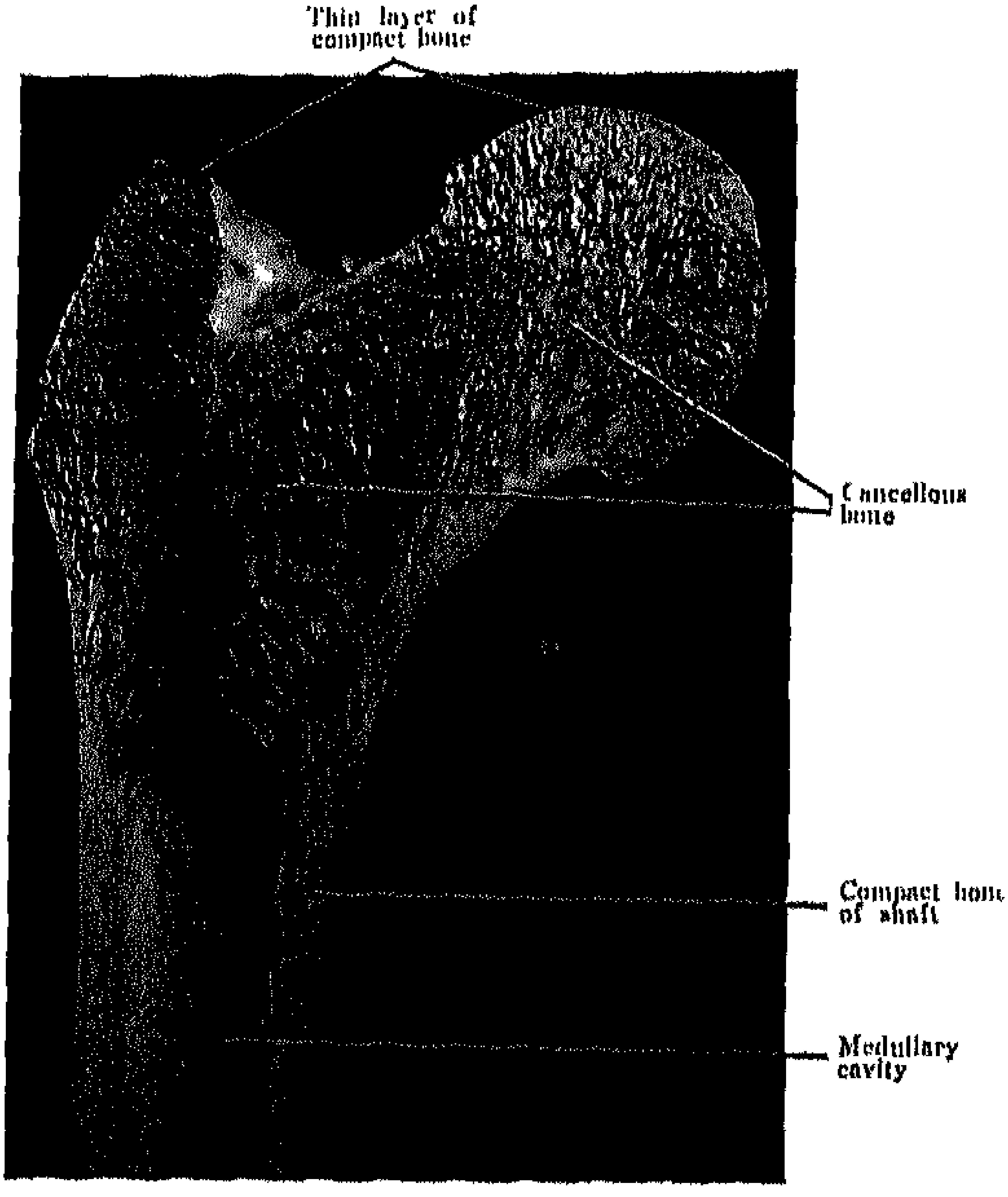


FIG. 87. Longitudinal section through the upper end of the femur of an adult. Photograph.

formed by *trabeculae* and *spicules* of bone which anastomose to form a latticework of bony tissue on the inside of the compact layer. This is known as *spongy* or *cancellous* bone. Spongy bone is also found in the bodies of irregular bones, and in the narrow strip of spongy tissue between the inner and outer plates of the flat bones of the skull, where it is known as diploë. The relative proportions of these two types of bone vary according to the needs for strength or lightness of weight. The center of long bones shows a cylindrical space, the *marrow cavity.*

This cavity contains the *bone marrow* which consists of *reticular tissue, fat,* and *developing blood cells.* Marrow also fills the spaces in cancellous bone. In adult long bones, the blood forming tissue (red marrow) in the diaphysis is largely replaced by adipose tissue and the blood forming elements are restricted, more or less, to the areas of cancellous tissue at the extremities of the bones.

Bone is an extremely vascular tissue and, with the exception of the articular surfaces, is invested with a fibrous connective tissue covering called the *periosteum.* This tissue will be discussed in greater detail later. Lining the marrow cavity is a membrane, formed by the condensation of the connective tissue of the medullary cavity, called the *endosteum*.

Bone, instead of being a solid, homogeneous mass, is made up of numerous thin layers of bony *lamellae,* held together by means of a small quantity of cement substance. Their arrangement varies according to their location in the bone. Examination of a cross section from the shaft of a long bone shows four distinct lamellar arrangements:

EXTERNAL CIRCUMFERENTIAL LAMELLAE. A few layers extend around the entire periphery of the bone. Because of their loca-

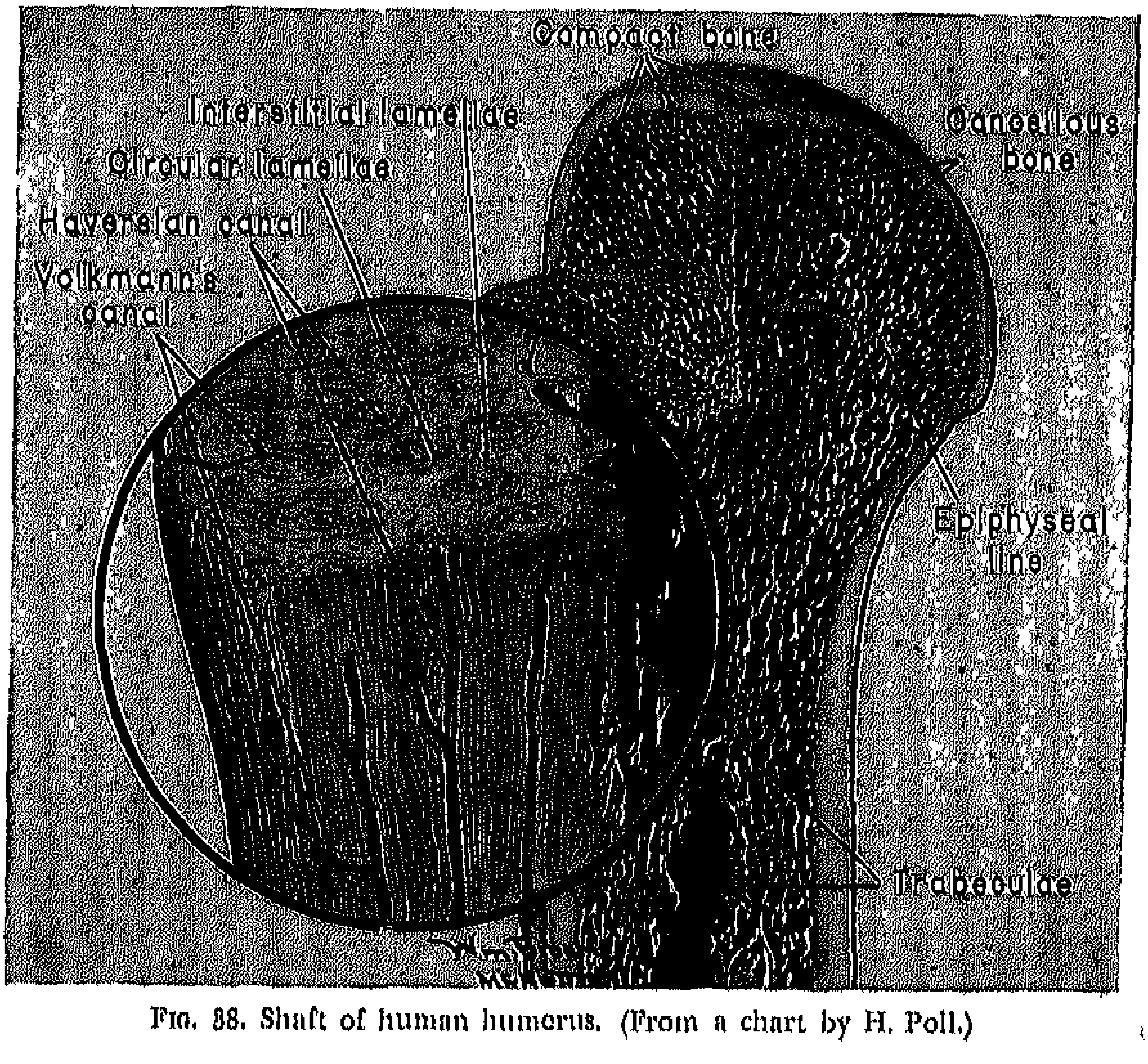


FIG. 38. Shaft of human humerus. (From a chart by H. Poll.)

tion and the fact that they are laid down by the osteogenic cells of the periosteal covering of the bone, they are called *external circumferential* (or *periosteal*) lamellae.

CONCENTRIC LAMELLAE. Internal to the external circumferential lamellae the cross section of bone shows numerous small channels, around which the bony substance is laid down in the form of concentric plates (*concentric lamellae*). The small channels run parallel to the long axis of the bone and are known as *Haversian canals*. They contain *blood* and *lymph vessels*, and *nerves*. Haversian canals are joined to one another by obliquely or laterally directed communicating canals.

INTERSTITIAL LAMELLAE. During growth in diameter of a bone, old Haversian systems may be partially resorbed and new ones formed. The remnants of the old systems fill the spaces between the new Haversian systems and are called *interstitial lamellae*. If the concentric lamellae of the Haversian systems could be removed, and the interstitial lamellae allowed to remain, a condition resembling spongy bone would result. The trabeculae and spicules of spongy bone possess a lamellated structure, but the lamellae are not organized into Haversian systems.

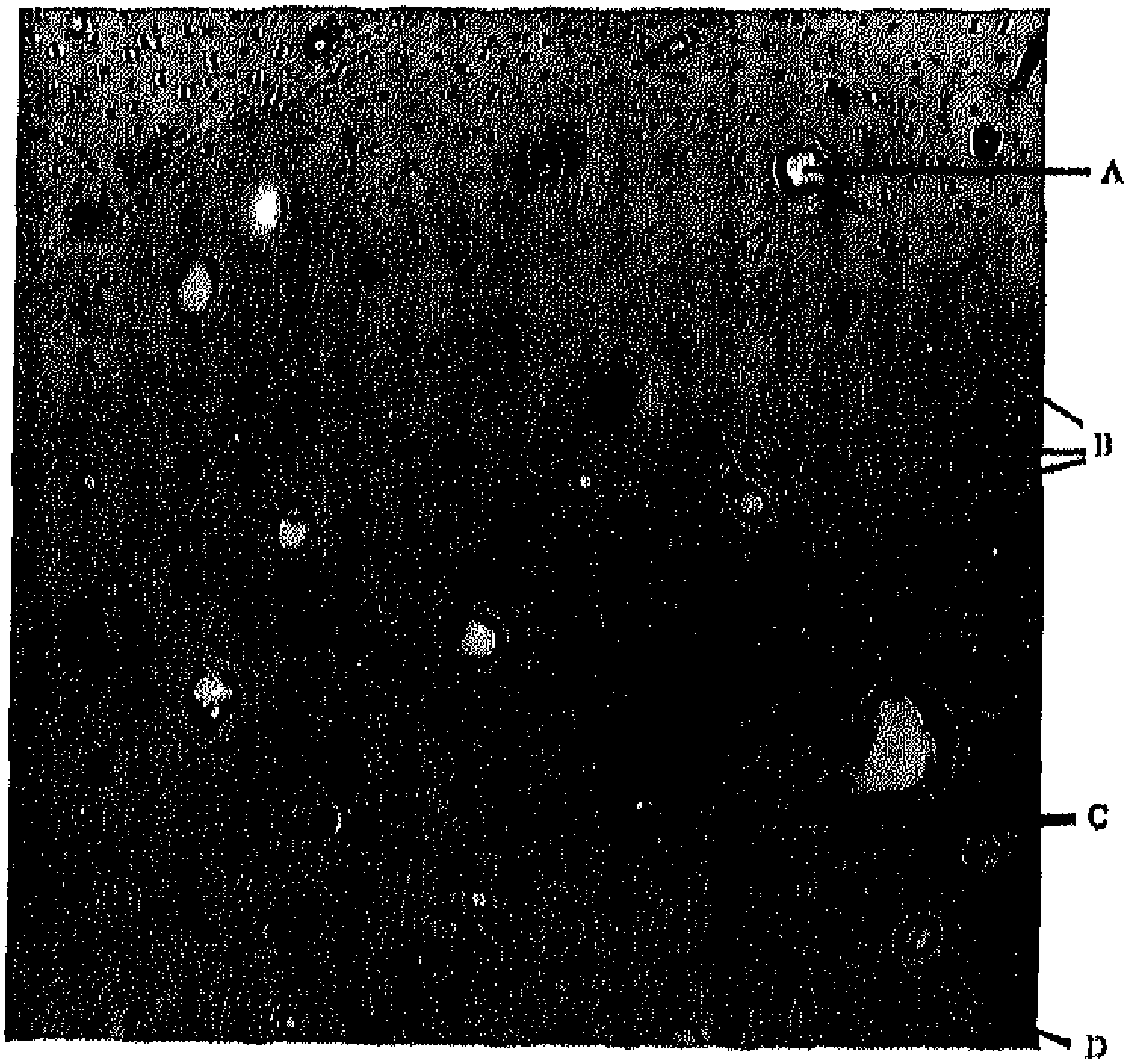


FIG. 30. Cross section of decalcified compact bone. (A) Haversian canal. (B) Osteocytes arranged between concentric bony lamellae. (C) Concentric lamellae. (D) Interstitial lamellae. The canaliculi do not show. Hematoxylin and eosin stain. Photomicrograph.

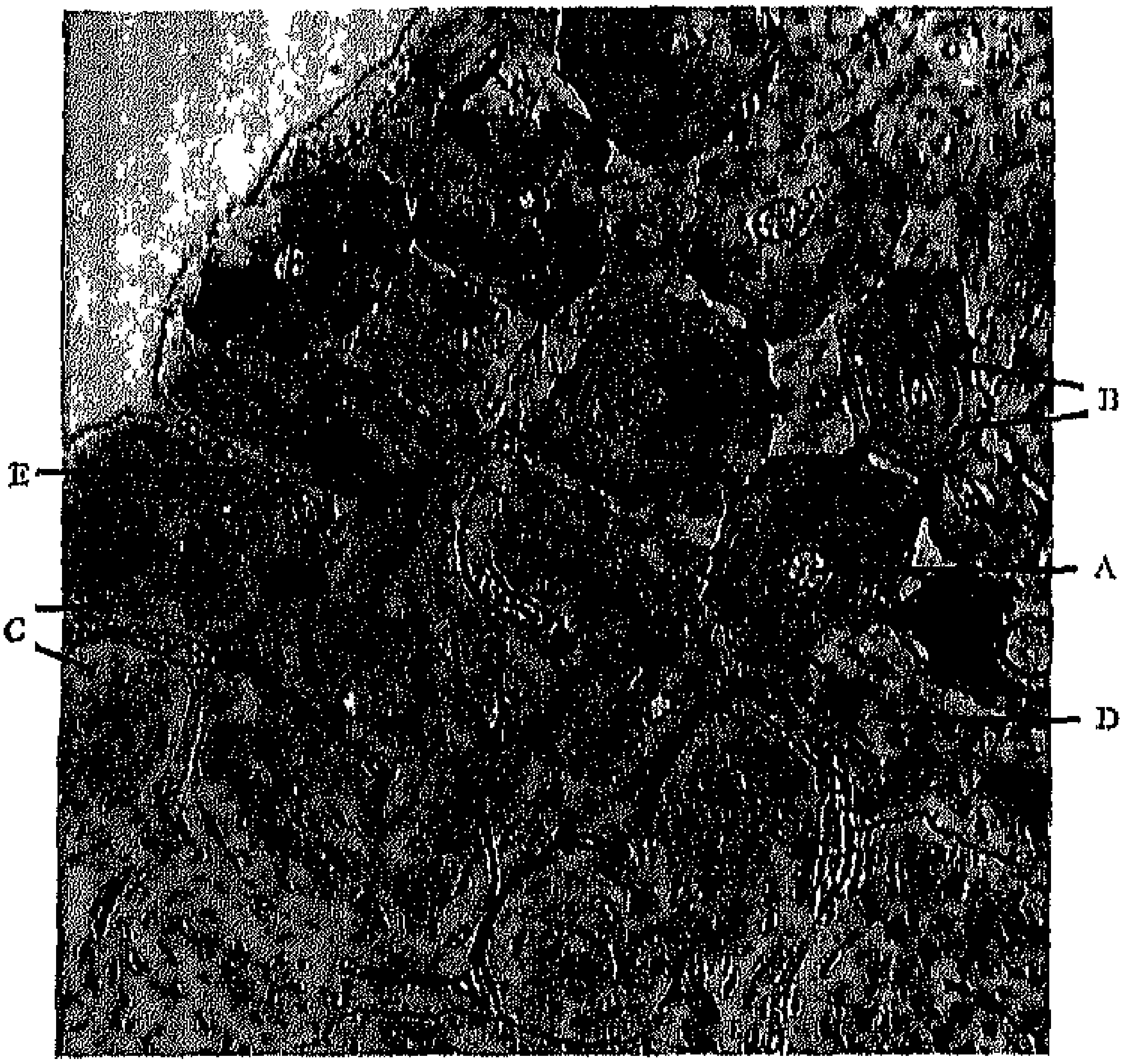


FIG. 40. Cross section of compact bone (not decalcified). (A) Haversian canal. (B) Concentric lamellae (C) Lacunae. (D) Interstitial lamellae. (E) Volkmann's canal. Photomicrograph.

INTERNAL CIRCUMFERENTIAL LAMELLAE. These are found on the inner aspect of the bone and are similar in arrangement and appearance to the external circumferential lamellae. They are laid down by the endosteum which lines the marrow or medullary cavity.

The *lacunae* are almond-shaped spaces found between the lamellae, although they also occur within the lamellae themselves. These spaces are joined to one another by numerous fine canals *(canaliculae)* which extend from the lacunae in all directions through the bony lamellae. They branch and anastomose freely so that the bone is filled with a network of extremely minute canals which carry nutrient materials. Bone cells, or *osteocytes*, are lodged in the lacunae and in living bone completely fill them. In prepared material, the protoplasm of the osteocytes shrinks and pulls away from the walls of the lacunae. Osteocytes are modified connective tissue cells and, like the cells of all other forms of connective tissue, are derived from the primitive mesenchyme. These cells possess a granulated cytoplasm which is more or less vacuolated in prepared sections, and a rounded nucleus which lies in the center of the cell. Delicate protoplasmic processes extend from the cytoplasm of the osteocytes and enter the canaliculae where they branch in the same pattern as the canaliculae. It is probable that these processes anastomose with the processes of adjacent cells. This results in the bone being filled with a network of living substance.

The lacunae which lie nearest to an Haversian canal communicate directly with the canal by means of their canaliculae. In an Haversian system, the continued communication of the osteocytes with one another, by means of their processes which occupy the canaliculae, and of the cells in the interstitial lamellae with those at the boundaries of the Haversian systems, insure the connection of all the cells with the sources of nutritive supply.

Small canals pierce the external and internal circumferential layers of bone and join the Haversian canal. They are known as Volkmann's canals and they differ from the Haversian canals in not being surrounded by concentric lamellae. They do not form an independent system, but with the Haversian canals they provide a series of channels by means of which blood vessels, lymphatics, and nerves are distributed throughout the bone.

Fibers are present in all parts of the bony matrix and can be demonstrated by suitable methods. In a single lamella the fiber bundles are arranged parallel to one another. In an adjacent lamella, the fiber bundles are also arranged in parallel, but they lie at right angles to those of the neighboring lamellae. This is especially noticeable in the Haversian systems. Besides the fibers found within the lamellae, there

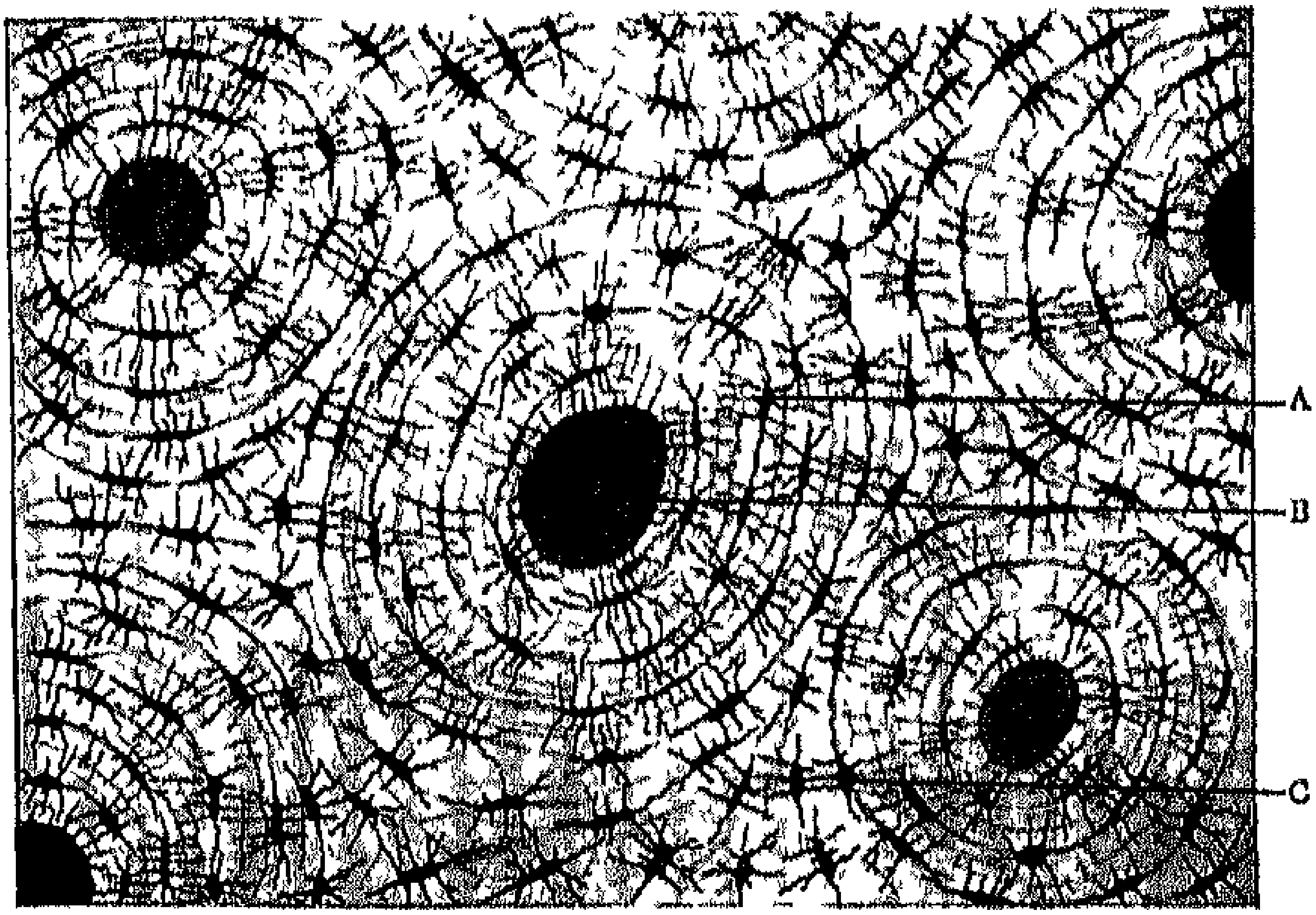


FIG. 41. Transverse section of compact bone. (A) Concentric lamellae of Haversian system with lacunae and canaliculi. (B) Haversian canal at the center of an Haversian system. (C) Interstitial lamellae.

are also bundles of collagenous and elastic fibers derived from the periosteum, which enter the bone at right angles to its long axis. They are known as *perforating fibers* or *Sharpey's fibers*. They penetrate the outer bony lamellae and may extend into the interstitial lamellae, but they do not enter the Haversian systems. These fibers are especially numerous where tendons are attached to bone.

Applied to all parts of bones, except their articular surfaces, is a layer of connective tissue known as the periosteum. It consists of collagenous fiber bundles intermingled with numerous elastic fibers. The fibers of the outer part of the periosteum are loosely arranged and blend with the surrounding connective tissue. They give support to numerous blood vessels and lymphatics, for which reason the outer layer is sometimes referred to as the *vascular layer*. The fibers of the periosteal tissue which lie upon the surface of the bone are more regularly arranged, as well as being more compactly interwoven, and form what is known as the *fibrous layer*. When bone is injured to the extent that it needs to be replaced, the cells of the fibrous layer, especially those which lie immediately on the surface of the bone, become *bone formers (osteoblasts)* and restore the bone that has been removed or destroyed in the injured area; hence the deep portion of the periosteum, in which these cells are located, is sometimes referred to

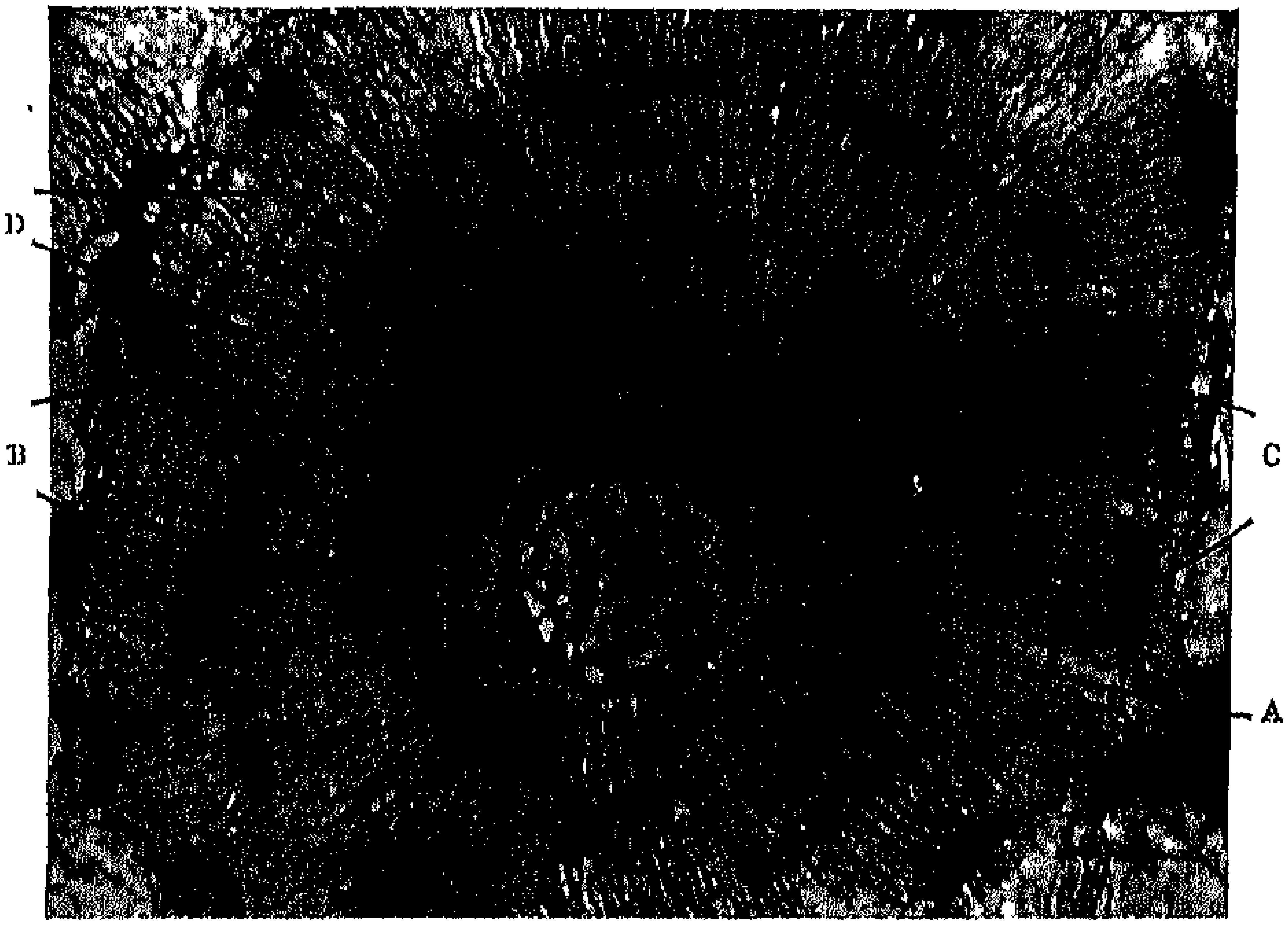


FIG. 42. An Haversian system, undecalcified compact bone. (A) Haversian canal. (B) Concentric lamellae. (C) Lacunae. (D) Canaliculi. Photomicrograph.

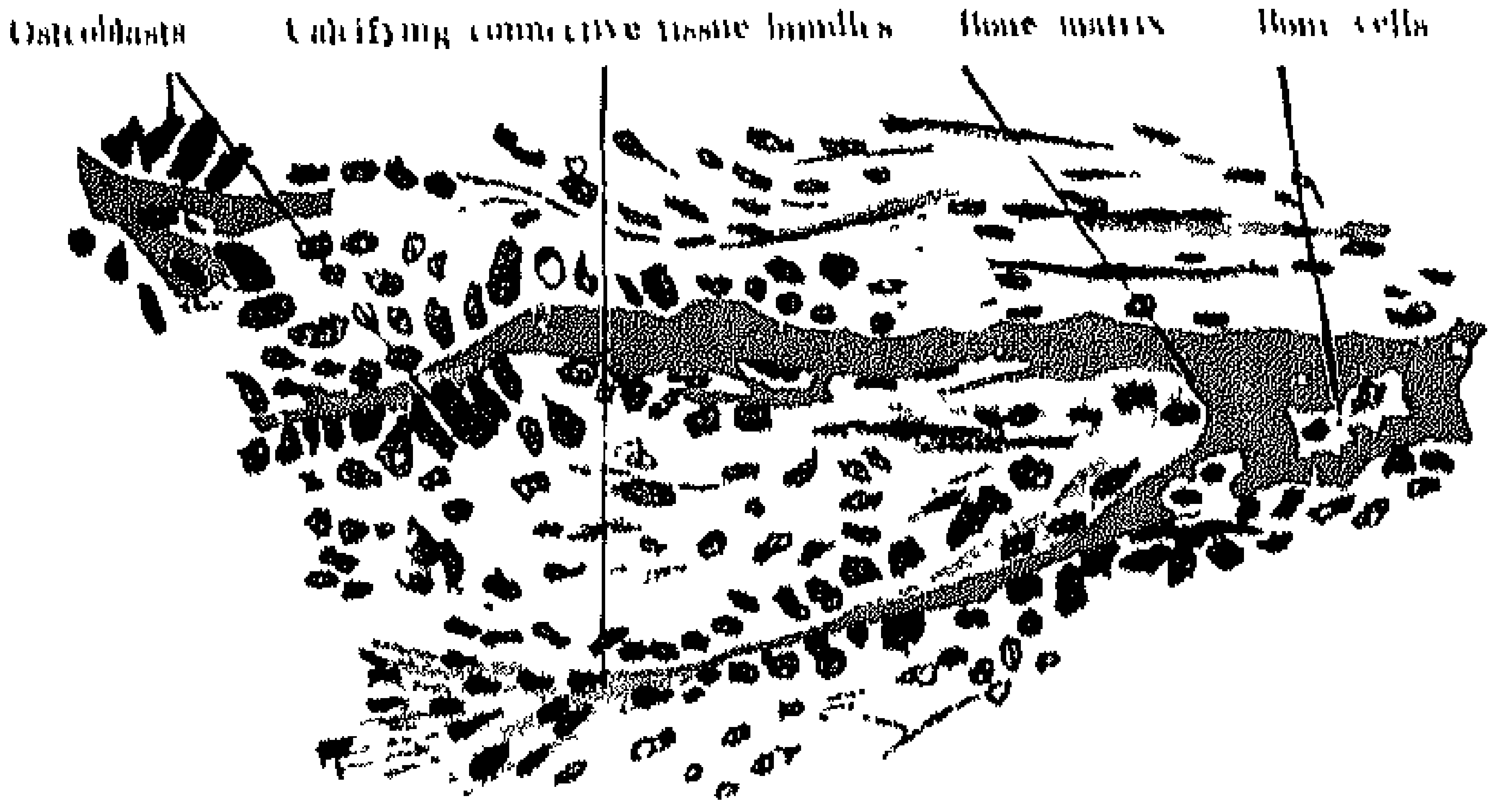


Fig. 43. Developing intramembranous bone. From the mandible of a human embryo of four months.

as the *osteogenic layer*. Under normal conditions the cells of the osteogenic layer remain inactive in adult bone.

Formation of Bone

Bone always develops in relation to either an embryonic or adult type of connective tissue. Certain bones, namely those which form the vault of the cranium, the bones of the face, and mandible and probably the clavicle, arise directly within the membranes in which they are located. Bones of this kind are known as *membrane bones*, and the process by which bone develops in membranes is called *intramembranous bone formation*. A second type of bone development is known as *endochondral* or *intracartilaginous bone formation*. In this type, the original membranous matrix is converted into cartilage, which in turn is removed and replaced by bone. The bone produced by these two methods is histologically the same, the terms merely indicate the method of development. The first bone formed by either method is always spongy or cancellous, only in later development is it changed into compact bone by remodeling of the existing bony material.

INTRAMEMBRANOUS BONE FORMATION. The most typical examples of intramembranous bone formation are to be found in the formation and growth of the bones of the cranial vault (frontal, parietal, and upper portion of the occipital bones). Immediately preceding the formation of bone, the mesenchymal cells in the area proliferate and many small blood vessels invade the tissue. There is a tendency for the mesenchymal cells to group themselves together in elongated clusters throughout this area. In the region where this change is taking place, the connective tissue fibers become swollen. The connective tissue cells change and assume a more or less cuboidal shape

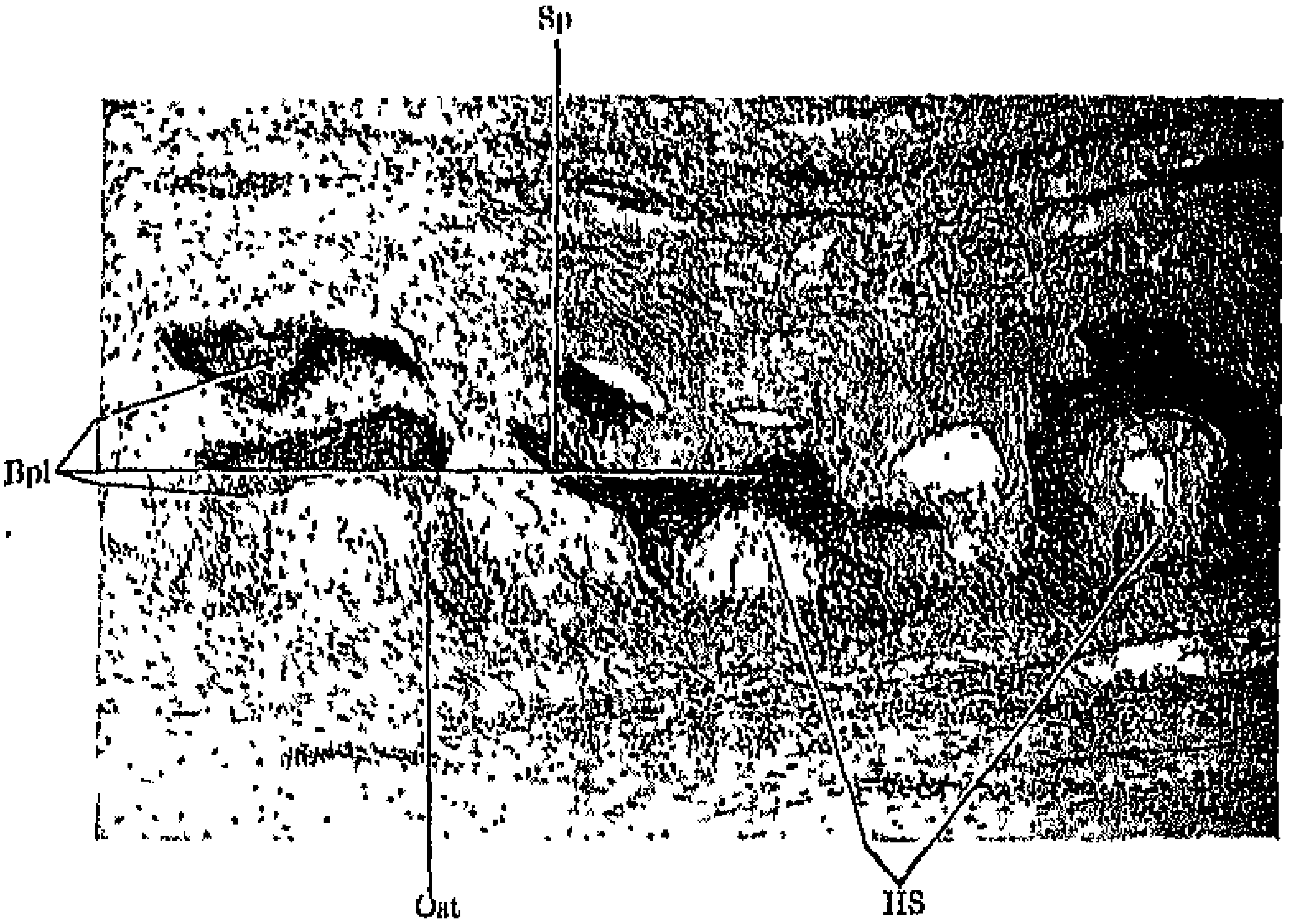


FIG. 44. Bone formation, early stage. (Bpl) Bony plates. (HS) Haversian spaces with blood vessels about to be completely enclosed by the growing bone. (Ost) Osteoblasts laying down osteogenic material on a small plate of bone. (Sp) Spicule continuing the growth of the bony plate into the surrounding periosteal tissue. Photomicrograph.

and the cytoplasm takes a more basophilic stain which characterizes them as bone forming cells or *osteoblasts.* The osteoblasts produce certain changes in the ground substance, which becomes a thickened hyalinlike material called *ostein (preosseous material: osteoid)* which completely masks the fibers embedded in it.

The osteoblasts multiply and are arranged in a regular manner along the borders of the preosseous material or ostein, and also along the swollen fibers. Here they continue to deposit ostein, thus increasing the size of the preosseous area which, as the ostein is laid down along the fibers, acquires an irregular outline. The ostein which is deposited in this manner forms the organic base for the matrix of the bone. Following the formation of the organic portion of the matrix, calcium salts in a finely granular condition are deposited in its substance. In this manner a number of bony spicules and plates, irregular in outline and varying in size, are formed in the connective tissue.

Two distinct processes thus occur in the formation of bone: (1) The production of ostein by the osteoblasts. (2) The deposit within this material of calcium and other inorganic salts. The calcium salts are not merely precipitated in the preosseous substance, as in the calcification of cartilage, but assume a regular and intimate relation to the material in which they are deposited. This is known as *ossification.*

The growth of bone is due to the osteoblasts depositing additional layers of ostein on the surface of the bony plates and spicules. In prepared sections, the calcified area (bone), which stains a deep red, is surrounded by a narrow border of faintly staining, homogeneous ostein on which the osteoblasts rest.

The secretion of preosseous material takes place only from that portion of the cell which is adjacent to the bone. Certain osteoblasts seem to lose their power to produce ostein and become inactive. When this occurs, the neighboring osteoblasts soon deposit a layer of ostein about these cells and in this manner they become embedded in the matrix. These cells, which occupy the lacunae in the bony material, are now called bone cells or *osteocytes.* The canaliculae are formed as the ostein is laid down around the delicate processes of the osteocytes.

The examination of a section of developing bone will reveal the fact that the lightly stained border of ostein does not extend all the way around the bony plate. Certain areas appear in which it is not present.

As new bone is formed, the plates are soon joined together on the inner side to form a continuous bony layer. On the outer side the osteoblasts continue to deposit bone along the radiating fibers, forming spicules and trabeculae. These bony projections grow toward one another and finally unite, enclosing large spaces (*Haversian spaces*) which contain primitive marrow and blood vessels. This process is repeated and the bone increases in thickness.

The bone on the cerebral side does not remain, but is removed by a process of resorption at a rate which corresponds to the extension of the bone in the outward direction. This removal of the inner portion of the bone, along with the continued deposition of bone at the edges of the skull bones, increases the size of the cranial cavity, thus paralleling the growth of the brain. The process by which bone is resorbed is not well understood. Certain giant, multinuclear cells, which are called *osteoclasts*, are thought to play a part in bone resorption.

After bone has reached the limit of its growth, resorption ceases. On the inner or cerebral side, the tissue becomes dense bone by the filling of the Haversian spaces with concentric bony lamellae. This remains as the inner plate. (The primitive marrow cells in the Haversian spaces become osteoblasts. These cells become arranged about the walls of the spaces and deposit preosseous material in a series of concentric bony layers until the Haversian spaces are completely filled with bony material, except for the center which is occupied by lood and lymph vessels and nerves.) The spicules of the outer portion ' the bone unite and form Haversian spaces, which are likewise filled ' concentric lamellae of bone, the dense bone of the outer plate thus ing formed.

In the areas between the plates, the spaces between the bars and spicules of the spongy bone remain unaltered; or where they may have been obliterated by the formation of concentric layers of bone,

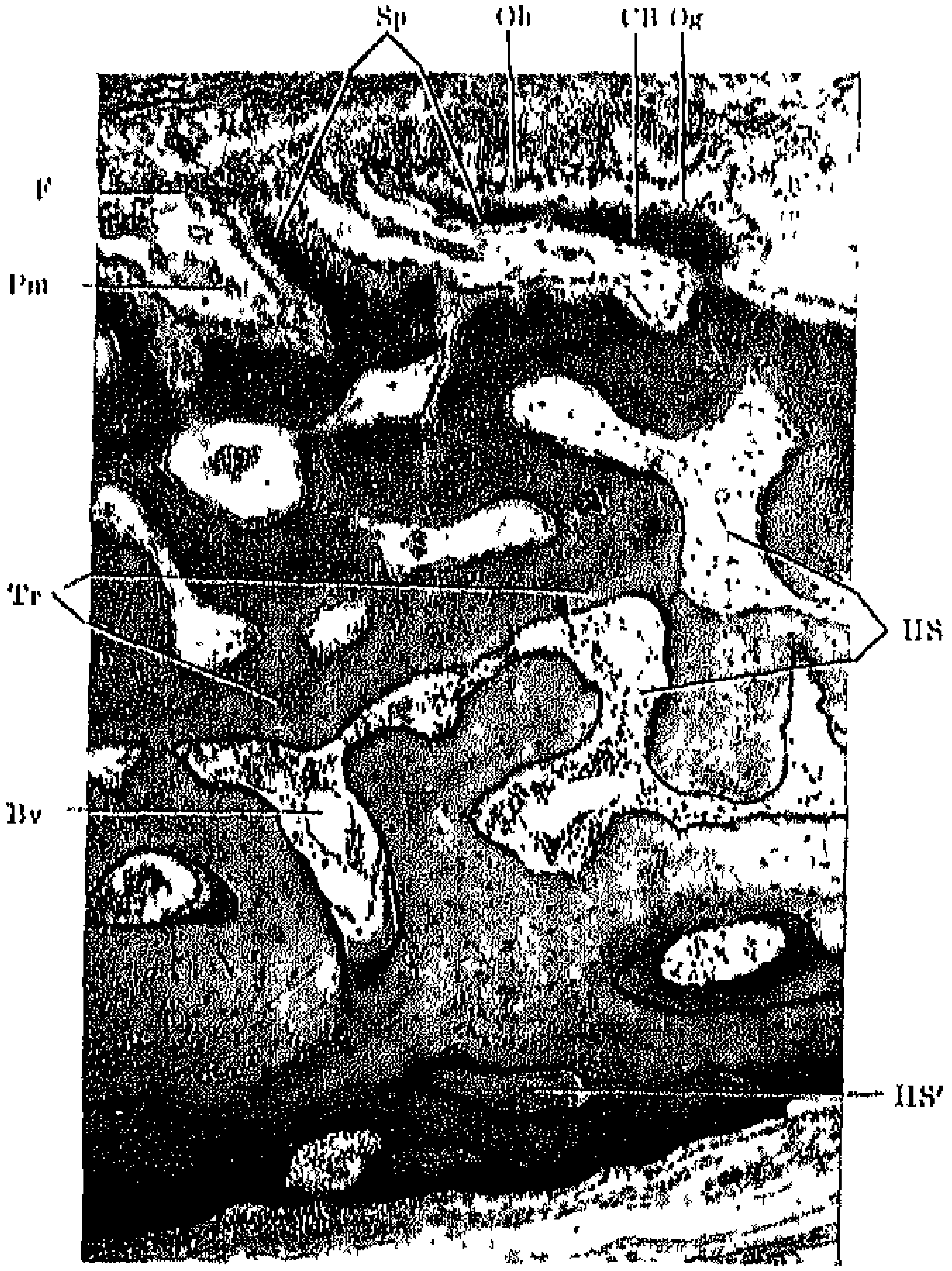


Fig. 45. Intramembranous bone. (Bv) Blood vessel in Haversian space. (CB) Calcified portion of bony spicule. (F) Modified connective tissue fibers along which new bone-material will be deposited. (HS) Haversian spaces. (HS') Haversian space completely filled with bone by the action of osteoblasts (a typical Haversian system). (Ob) Osteoblasts. (Og) Uncalcified bony material (osteogenic substance). (Pm) Connective tissue (external periosteum) being transformed into primitive marrow. (Sp) Spicules extending into the connective tissue forming the external periosteum. (Tr) Bony trabeculae. Photomicrograph.

they are again reopened by the resorption of this bony material. The tissue in this region remains as the spongy bone of the diploë. The spaces in the diploë are filled with the cells and fibers which form

ENDOCHONDRAL BONE FORMATION. All parts of the skeleton, with the exception of those which have been referred to as membrane bones, first appear in the embryo as embryonic hyaline cartilage. As the development of the embryo progresses, these cartilages are replaced by bone, except on the articular surfaces of the bones. The process by which this takes place is known as *endochondral bone formation*. The cartilages which form the early embryonic skeleton, moreover, serve to give direction to the growth of the bones by which they are replaced, and to a certain extent, influence their form. As the term endochondral bone formation indicates, this type of bone is developed within the cartilage, but it must be realized that in this process, the cartilage is not converted into bone. The cartilage is first removed and is replaced by bone. Bone formation in this case is essentially similar to intramembranous bone formation. The fate of the cartilage cells which are released with the breakdown of the cartilaginous matrix is not known. They may revert and become fibroblasts; some of them, at least, undoubtedly degenerate and are phagocytized by connective tissue cells or blood cells of the bone marrow.

To understand this type of bone formation, it is essential to realize that as the first changes are taking place in the center of the cartilage within the shaft of the long bone, another series of changes are occurring almost simultaneously at the periphery of the cartilage. These latter changes, involving the perichondrium (shortly to be called periosteum), result in typical intramembranous bone formation and produce a "collar" of bone around the outer margin of the cartilaginous mass.

In the center of ossification, the cartilage has become honeycombed by the resorption of some of the cartilage between the spaces occupied by the cartilage cells. In the meantime, the cells and fibers of the osteogenic layer of the periosteum, accompanied by a blood vessel, organize to form a *periosteal bud*. This forms a channel through the intervening bone collar and cartilage by the absorption of their substance and breakdown of the thin walls of the lacunae. The cavity thus formed is called the *primary marrow space*. From the tissue of the periosteal bud is derived the cells and constituents of the *primary bone marrow* which soon fills the primary marrow space.

As the periosteal bud invades the bone and cartilage, it carries with it the potential bone forming cells or osteoblasts. The walls of the primary marrow cavity are quite irregular owing to the spicules of calcified cartilage which still remain and project into it. The osteoblasts arrange themselves along these cartilaginous spicules and bars, nd deposit bone upon them in the same way as bone was deposited long the fiber bundles in intramembranous bone formation.

In the meantime osteoclasts, also derived from the cells of the primary marrow, come into contact with the newly formed bone and begin its resorption. Thus bone formation and the destruction of the newly formed bone are going on at the same time.

The calcification of the cartilage, with the accompanying changes in the cells and the enlargement of their lacunae, continues in all directions from the center of ossification. This results in the formation of other primary marrow spaces which are finally joined in a single large cavity in the diaphysis, known as the *secondary marrow space*. When the process has extended to the subperiosteal bone, the cartilage in this area has disappeared, the subperiosteal bone forming the outer boundary or wall of the secondary marrow cavity.

The calcification of the cartilage continues toward the epiphysis. Here the cartilage cells divide transversely so that they become arranged in rows which run parallel to the long axis of the bone. The cartilage

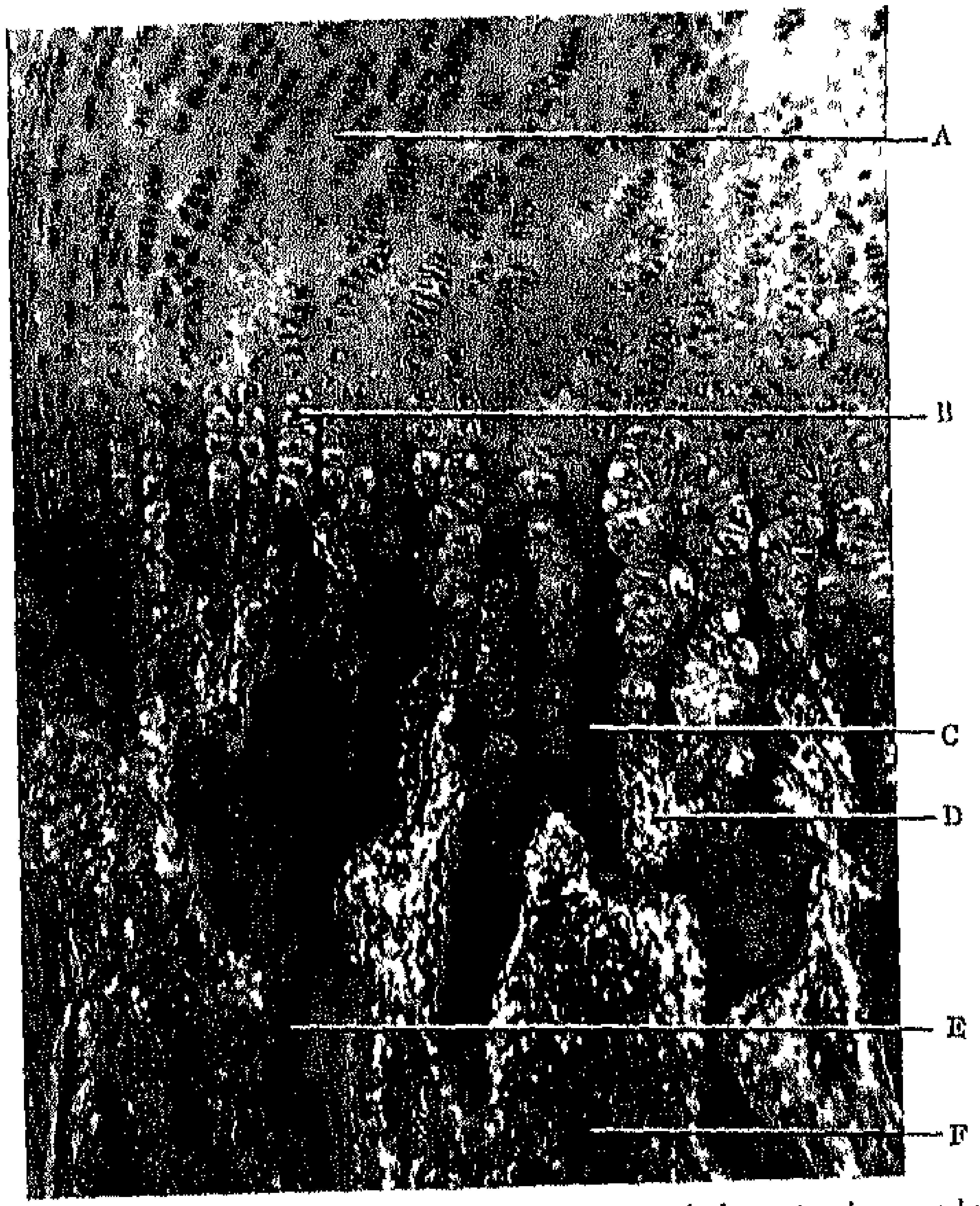


FIG. 46. Longitudinal section of a portion of a human phalanx to show endochondral bone formation. (A) Embryonic cartilage. (B) Cartilage cells arranged in columns. (C) Calcified cartilage. (D) Primary marrow space. (E) Spicule consisting of calcified cartilage with bone deposited about it. (F) Secondary marrow space.

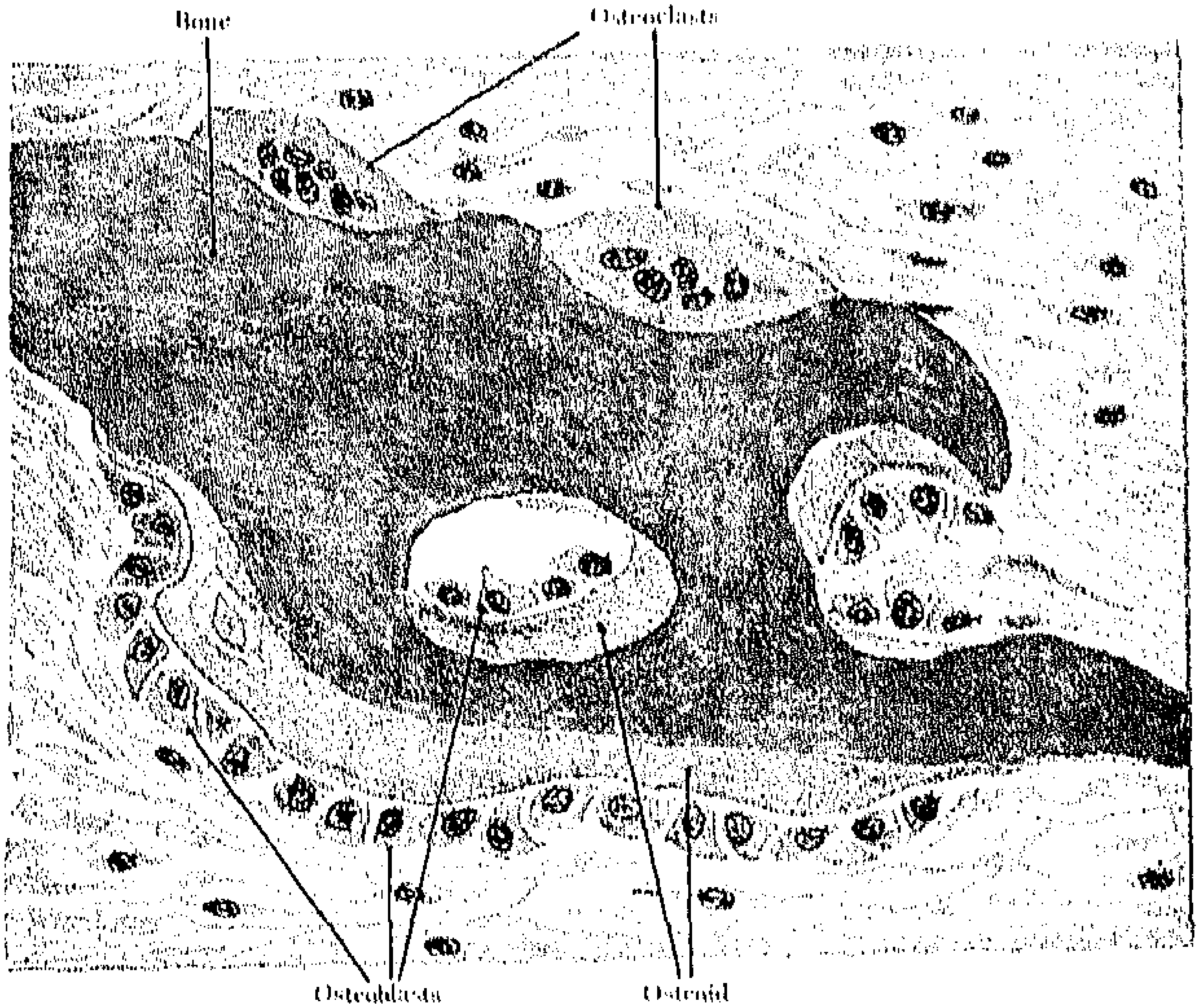


FIG. 47. A drawing (semi-diagrammatic) showing osteoblasts and osteoclasts. (After LeGros Clark.)

walls break down between the enlarged lacunae, forming spaces of considerable size which are separated by the calcified cartilage remaining between the rows. These primary marrow spaces are invaded by osteogenic tissue (primary marrow) which extends into them from the secondary marrow space. The calcified cartilage between the primary marrow space extends in the form of spicules into the secondary marrow space. Osteoblasts are arranged along the borders of these spicules and form the layers of bone by which the spicules are enclosed. The spicules are then resorbed by the action of osteoclasts and other agencies which are active in the removal of bone. By the continuation of this process, the secondary marrow cavity (marrow cavity of the bone) is extended in the direction of the epiphyses.

The bone increases in length by the division of the cells in the embryonic cartilage of the epiphyses, and the deposit of additional matrix about them. As the length of the diaphysis increases, the periosteal tissue by which it is surrounded becomes periosteum, and the subperiosteal bone is correspondingly lengthened. It also increases in thickness by the continued addition of new layers of bone on its outer surface. This bone is formed by the action of the cells (osteoblasts) of the osteogenic layer of the periosteum, a process which is similar in all respects to that observed in the development of intramembranous bone.

As the subperiosteal bone about the diaphysis increases in thickness, the process of resorption becomes active on its inner surface with the consequent enlargement of the diameter of the marrow cavity. A number of periosteal buds are formed which push their way into the marrow cavity, carrying with them additional osteogenic tissue and blood vessels. This process of growth and resorption of the bone about the diaphysis continues until it has attained its adult size and condition. The blood vessels and their branches, which remain in the bone, occupy the spaces that later become the Haversian systems.

The epiphyses of the long bones retain their cartilaginous condition until after birth. Blood vessels, accompanied by osteogenic tissue, invade the cartilage and form centers from which the process of ossification extends in all directions. Several of these centers are formed in the epiphyses of the longer bones; in the smaller bones only a single center is present. As the lacunae are enlarged, and become confluent, bars and spicules are formed on which the bone is laid down in the manner already described. These interlacing bars and spicules remain, or if resorbed, they are later replaced by the formation of new bars and spicules. This results in the production of the spongy bone of the epiphysis. The osteogenic tissue spreads through the spaces in the spongy bone and becomes the bone marrow.

Since the ossification of both the diaphysis and epiphysis takes place before the bones have attained their adult condition, provision is made for their continued growth in length by a plate of cartilage *(epiphyseal plate)* which remains between them. The position of this cartilaginous plate is indicated on the surface by a shallow groove *(epiphyseal groove)*. The continued growth of the bone in length is accomplished by the division of the cartilage cells and the formation of new matrix; in the portion of the plate toward the epiphysis, the cartilage being replaced by bone on the side toward the diaphysis, in the manner already described. As the formation of spongy bone takes place within the epiphysis, its growth is continued by the division of the cartilage cells and the addition of a matrix at its surface.

BLOOD SUPPLY OF BONE

Bone is an extremely vascular tissue. Numerous small vessels derived from the periosteal vessels enter the Haversian canals of the subperiosteal bone by way of Volkmann's canals. These vessels continue into the marrow cavity where they form capillary networks. They anastomose with capillaries derived from the medullary arteries. The medullary (nutrient) artery enters the shaft of the long bones near the center of the bone. It passes obliquely through the compact bone of the shaft, where it communicates with the arteries of the Haversian canals and on entering the marrow space it divides into an ascending and descending branch. These vessels in turn divide and eventually open into wide sinusoidal capillaries. Accompanying the medullary artery are nerves, veins and lymphatics. In view of the subsequent study of pathology, it is important at this point, to call attention to the peculiarity of the vascular supply to the ends of long bones. (The blood supply to long bones has been worked out on fetal material and bones of growing animals and is reported by H. A. Harris.) Because of the very poor anastomoses between the terminal vessels of the arteries of the diaphysis, these vessels for all practical purposes may be thought of as end arteries which do not extend across the epiphyseal line. The epiphysis, on the other hand, is supplied by the articular branches of vessels in the near vicinity. These arteries are not end arteries, but tend to anastomose freely. Thus lesions in the shaft and the epiphysis are very typical (localized in the shaft; general, widespread in the epiphysis).

BONE MARROW

Bone marrow is a soft cellular tissue which is found in the medullary cavity of long bones, around the blood vessels of the large Haversian canals, and filling the intertrabecular spaces of spongy bones. The supporting framework of bone marrow is a reticulum which, except for its wide meshes, is similar to that which forms the framework of the lymphoid organs. The endosteum by which the marrow cavities are lined is not a definite membrane, but a condensation of the reticular tissue on the inner surface of the bone. The reticular cells are fixed macrophages which, when separated from the reticulum, become the free macrophages (histiocytes) of the tissue spaces.

Two kinds of bone marrow are recognized: (1) *red* and (2) *yellow*. In the bones of the fetus and in children the only marrow present is *red marrow*. It is formed by a rich variety of cells, supported by the reticular tissue framework, constituting the myeloid elements from which the formed or cellular elements of the blood are derived. In the fetus the liver, spleen, and lymph glands contribute to the formation of the cells of the blood. These organs lose their hemopoietic function shortly after birth, the cells which are found in the blood stream being formed in the red marrow. In the adult, the red marrow occupies the spongy bone in the epiphyses of the long bones, the bodies of the vertebrae, the ribs, the sternum, and the diploë of the flat bones. The red marrow in long bones of the adult is restricted to the ends of the bones, that in the diaphysis (marrow cavity) being replaced by *yellow marrow*. Yellow marrow contains large masses of fat, by which the cells characteristic of bone marrow have been displaced. (Fat in red marrow consists of single cells found among the other cells of the tissue.) Thus in the adult, the red marrow is the most important hemopoietic organ of the body.

The blood vessels in bone marrow end in capillaries that communicate with thin-walled sinusoids, through which the blood passes before it enters the veins. The cells forming the walls of these sinusoids are thought by some to be a specialized kind of endothelium. They are regarded by others as flattened reticular cells which have assumed the form and position of endothelial cells. Whichever may be the correct view, the cells in the walls of the sinusoids are phagocytic and may detach themselves from their connections with the other cells and enter the blood stream or tissue spaces as free macrophages.

CELLS OF BONE TISSUE

OSTEOBLASTS. Osteoblasts are derived from the direct transformation of connective tissue cells (mesenchymal cells). The mesenchymal cells increase in size and become more or less cuboidal, at the same time, however, retaining their processes. These processes frequently anastomose with those of adjacent cells, and also may extend into the newly formed osteogenic substance. The cytoplasm is finely granular and reacts intensely to the basic stains. The nuclei are large, round and usually located to one side of the cell.

The osteoblasts are arranged in a regular manner on the surface of the matrix, although they do not lie close to one another as do the cells of an epithelium, but are separated to make way for the fibers from the surrounding tissue which is being incorporated in the substance of the bone. Osteoblasts become flattened and lie close to the surface of the bone when they are no longer actively secreting ostein. After bone growth has ceased, it is probable that the osteoblasts are transformed into fibroblasts. New osteoblasts can be formed at any time from mesenchymal cells of the neighboring connective tissue.

The exact role that osteoblasts play in the deposition of calcium and inorganic salts in the organic matrix is unknown. This deposition is not due to the direct activity of the cells, although it is probable that they produce substances which enable the organic matrix to withdraw inorganic material from the surrounding fluids.

OSTEOCLASTS. Associated with the areas in which resorption of bone is taking place, there are usually found certain giant, multinuclear cells called *osteoclasts*. These cells lie close to the surface of the bone and are frequently found in deep depressions, or bays, in the bone *(Howship's lacunae)*. Their origin is unknown, but it is likely that they may be derived from undifferentiated cells of the osteogenic tissue. These cells are characterized by their acidophilic cytoplasm (stains red with eosin) and the number of their nuclei, which is extremely variable (2 to 20 or more).

Various ideas are held concerning the part played by the osteoclasts in the resorption of bone; some observers doubt whether these cells have any relation to the process by which bone is removed. Certain facts, however, may seem to indicate that osteoclasts are concerned with bone resorption: they are found only in the areas in which the resorption of bone is taking place, they frequently lie in depressions which they appear to have hollowed out in the surface of the bone, and their staining reaction is acidophilic--a characteristic of cells which are capable of producing the acid substances necessary for the removal of calcium salts. When osteoclasts lying in Howship's lacunae are examined with the higher powers of the microscope, delicate processes are seen extending from the cell to the surface of the bone. There is some reason for believing that these "processes" have been misinterpreted, that actually they are the protoplasmic walls of vacuoles which are filled with fluids resulting from the reduction of the organic matrix of the bone by a proteolytic enzyme released by the osteoclast.

On the other hand, the number of osteoclasts in any given area is not enough to account for the rate at which the resorption of bone takes place; also, bone may be resorbed without osteoclasts being present, as in fractures where small fragments of bone are removed. Other factors are undoubtedly involved. The greater part of the inorganic constituents of the matrix is probably removed by acids present in the fluids by which the bone is bathed in the areas where resorption is taking place. The osteoclasts may be the agents that remove the organic ground substance of the matrix after the inorganic constituents have been disposed of.

OSTEOCYTES. Osteoblasts which are embedded in the bony matrix are called *osteocytes*. These cells have a granular cytoplasm which stains faintly basophilic. The nucleus is oval in shape and large. The chromatin particles are large and one or two nucleoli are present.

SUMMARY OF CHARACTERISTICS OF CONNECTIVE TISSUES

COMPOSITION. Cells
Fibers
Matrix

METHOD OF CLASSIFICATION. Based principally on consistency of the matrix and types and arrangement of fibers

Characteristics of the Fibers of Connective Tissue

Name	*Structural Characteristics*	*Location*	*Physiochemical Properties*
ollagenous or white fibers	When unstained, fibers appear white Fibers fine and always occur in bundles (exception is in mesenchyme where fibers are first forming) Fibers are wavy and do not branch	Predominates in loose and dense areolar tissue Tendons and fascias Scattered throughout body in connective tissue septa, capsules, etc.	Low refractive index Yields collagen when boiled Soluble in weak acids and alkalies Digested by acid pepsin Does not stain black with silver
lastic or yellow fibers	When unstained fibers appear yellow Individual fibers are thicker than individual collagenous fibers Fibers branch and anastomose Cut ends of fibers curl	Ligamentum nuchae Walls of blood vessels and wherever there is need for elasticity	High refractive index Yields elastin when boiled Resistant to weak acids and alkalies Slowly digested by pepsin and trypsin Does not stain black with silver Stains black with Verhoeff's elastic tissue stain
eticular or argyrophil fibers (called reticular because of their arrangement; called argyrophil because they stain with silver)	Fiber fine—branch and anastomose	Forms the stroma of all lymphoid organs, bone marrow, and tunica propria of alimentary tract	Intermediate refractive index Less resistant to the action of weak acids and alkalies Resistant to the action of pepsin and trypsin Stains black with silver stains

MORPHOLOGICAL CHARACTERISTICS OF CONNECTIVE TISSUES

Classification	*Cells*	*Fibers*	*Matrix*
Mesenchyme	Numerous Stellate-shaped	Early stage—no fibers Late stage—fibers single and not arranged in any orderly fashion	Fluid
Embryonal	Many but farther apart Stellate-shaped	Intercellular spaces filled with fibers that are arranged in bundles	Fluid
Fibrous Connective Tissue			
Dense areolar	Flat, stellate shaped fibrocytes Tissue compact and dense	Predominately collagenous fibers with some elastic fibers Collagenous fibers in bundles Bundles run in all directions	Fluid. Quantity small
Loose areolar	Same as above only tissue is loosely arranged *Found associated with adipose tissue*	Same as above	Same as above
Tendon (dense fibrous tissue)	Fibrocytes lie between fiber bundles and therefore show linear arrangement Cells thin and flat in profile	Fibers *arranged in parallel bundles*	Same as above
Ligamentum nuchae (dense elastic tissue)	Cells shorter and more oval than in tendon Cells lie between individual *fibers*, therefore are closer together and more numerous	Fibers arranged in parallel but not in bundles	Same as above
Adipose	*Cells have* "signet-ring" appearance Nuclei and cytoplasm pushed to one side by large mass of fat which cell contains	No fibers Cells held in position by *loose areolar tissue*	Same as above
Reticular	Stellate-shaped Stain poorly	*Fine fibers that form a meshwork* Stain selectively with silver	Fluid. Matrix contains many *lymphocytes*
Cartilage			
Hyaline	Fusiform and flattened in young cartilage Oval in *adult and old* cartilage Cells few and scattered *Nuclei definite* Cytoplasm clear	Collagenous, no specific arrangement, fibers masked by density and staining reaction of matrix	Semisolid. Quantity great
Elastic	Oval, few and scattered	Elastic fibers, no arrangement *Stains black with Verhoeff's elastic tissue stain*	Semisolid. Quantity large
Fibrous	Oval, few, arrangement is linear between the fiber bundles	Collagenous, arranged in wavy, parallel bundles	Fluid. Small quantity
Bone	Osteocytes—oval with fine processes *Osteoblasts—cuboidal, produce bone* Osteoclasts—large irregularly shaped multinuclear, destroy bone	Collagenous, *no arrangement* Masked by density of matrix	Hard and dense. Large quantity

7

Blood

Blood is a tissue consisting of *cells (formed elements)* which move freely in a fluid medium, the *plasma*. It is related to the connective tissues by its origin from the primitive mesenchyme, and also by the fact that, in the adult, its cells arise from the reticular tissue of the bone marrow and other blood forming organs.

The comparison between blood and the connective tissues may be made more exact if we regard blood as a tissue which, like other connective tissues, consists of *cells*, *fibers*, and a *matrix*. Because of the fluid condition of the matrix (plasma), the cells of the blood do not maintain a constant position in relation to one another. The fibers are in solution in the plasma *(fibrinogen)* and they become evident as fibers only when agents are employed to bring about their precipitation in the form of *fibrin*.

The total volume of blood is correlated with body weight and surface area. By the use of the "dye method," the volume has been estimated to be about 1/12 of the body weight. In the average adult this would amount to approximately 6000 cc.

It is relatively easy to reduce the composition of the blood to a diagrammatic representation as follows:

- Blood
  - plasma
    - serum
      - serum albumin
      - serum globulin
      - glucose extractives, calcium salts, sodium and potassium chlorides, carbonates, phosphates, etc.
    - fibrinogen
      - (yields fibrin)
  - formed elements
    - red blood cells
      - oxyhemoglobin
      - lecithin
      - salts
    - white blood cells
      - fibrin ferments
    - blood platelets
    - hemoconia or blood dust

Diagrammatic Composition of Blood
(Modified after Webster and Koch)

PLASMA

The plasma is a slightly alkaline fluid having a "soapy" feel and a yellowish color. It contains numerous organic and inorganic substances in solution, some of which vary in amount in changing physiological conditions. Others, such as calcium and blood sugar, are present in fairly constant quantities during normal health, although the blood sugar varies temporarily with sugar intake.

Plasma contains albumin, globulin and inorganic salts. One of the important globulins is fibrinogen which is diffused throughout the plasma. As long as the blood continues to circulate normally through the vessels, the fibrinogen remains in this diffused (solvent) condition. When the circulation is stopped, or the blood is removed from the vessels by injury, or otherwise, fibrinogen is precipitated in the form of fibrin which forms a network of interlacing fibers in which the formed elements are caught and held, the mass becoming a coagulum known as a clot. Other substances present in the plasma which are essential in the process of coagulation are: prothrombin, antithrombin,

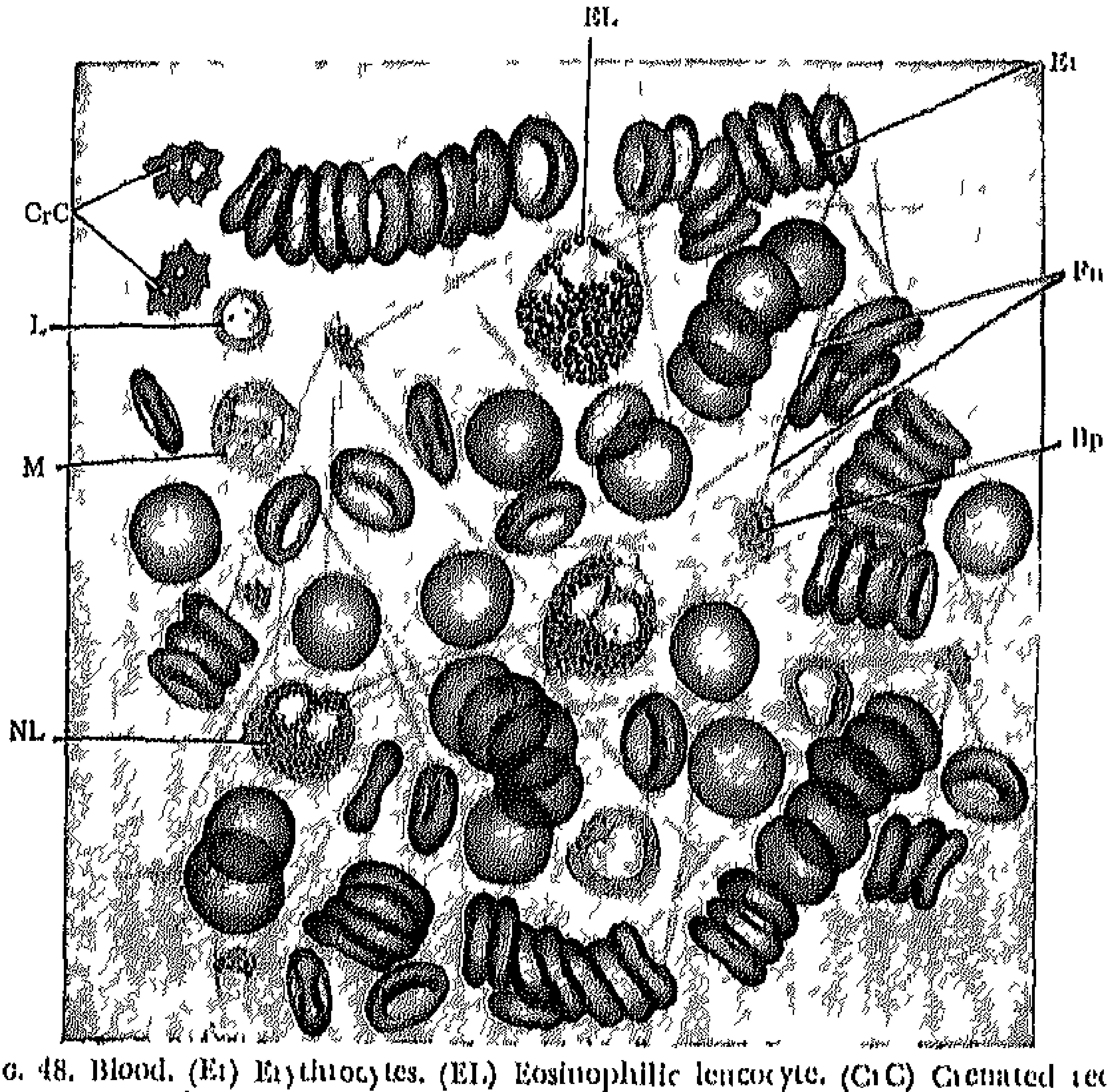


FIG. 48. Blood. (Er) Erythrocytes. (EL) Eosinophilic leucocyte. (CrC) Crenated red corpuscles. (L) Lymphocyte. (M) Monocyte. (NL) Neutrophilic leucocyte. (Bp) Blood platelet. (Fn) Fibrin fibers. (Redrawn after Schäfer.)

and calcium. When the fibrinogen, in the form of fibrin, and the formed elements have been removed from the blood, the residue is a thin, yellowish fluid, the *serum*. For a detailed discussion of the process of coagulation the student should consult a physiology text.

Functionally, plasma serves as a means of transportation for the formed elements of the blood. In it also are carried the materials which make clotting possible, as well as substances (for example, the products of the various endocrine glands) which are required by the tissue cells for the maintenance and regulation of their metabolic processes.

Where a clot has been formed, the serum appears as a clear, fluid exudate. In it are found *antibodies*, substances produced by the tissues as a protection against bacteria and certain other agents that are harmful to the body. Usually antibodies are formed only if the bacteria or agent is in the body and they are specific for the particular substance which called forth their formation. Therefore, to test for a specific antibody is to test for the particular disease.

CELLULAR OR FORMED ELEMENTS

The cellular, or formed, elements of the blood are: (1) the red corpuscles *(erythrocytes)*, (2) white cells *(leucocytes)*, (3) blood platelets *(thrombocytes)*, and (4) hemoconia *(blood dust)*.

ERYTHROCYTES

Erythrocytes, or red blood corpuscles, are highly specialized cells whose function is to carry oxygen from the lungs to the tissue and to bring back carbon dioxide. This is made possible by the hemoglobin (a complex iron-containing protein) which is found in the corpuscle and gives it its characteristic color. In the normal adult mammal the erythrocytes are formed from reticulo-endothelial cells of the bone marrow of vertebrae, ribs, sternum, flat bones and the proximal ends of the long bones. Sites for red blood cell formation in the fetus are the yolk sac, the liver and spleen. The length of the life of the red blood cell in a normal person is not known. However, Wearn, Warren, and Ames, basing their conclusion on the length of time transfused blood corpuscles survived in anemic patients, gave the range of their life span from 59–113 days (two to almost four months). When the corpuscles are no longer capable of functioning, they break into fragments which are ingested by phagocytic cells in the blood stream, the spleen, the hemolymph glands, the liver and the bone marrow. The pigment substances of the red corpuscles are utilized in the formation of bile.

Erythrocytes are called "corpuscles" because, unlike the leucocytes, they do not possess a nucleus. However, a nucleus is present in the cells *(normoblasts)* from which the red corpuscles are derived. In a few mammals, and in many of the lower animals, the erythrocytes retain their nuclei throughout life.

The red corpuscles are flattened, biconcave discs without nuclei. It is of interest that this biconcave shape offers the greatest possible surface area for the size of the cell. They appear dumbbell-shaped when cut in half and viewed edgewise. When viewed on their flattened surface, the corpuscle shows a thin central portion which appears lighter than the thickened marginal portions. While the biconcave disc shape is by far the most common seen in the circulating blood or in stained smears, bell- and cup-shaped cells have been described. These variations are most likely a modification of the biconcave form, due to certain external factors which influence the corpuscle.

In thin smears of freshly drawn blood, the cells have a greenish yellow color. The characteristic red color becomes evident when the cells are crowded together in the plasma.

Mature human red blood cells are not motile and their passage through the vascular system is entirely "passive." However, they are soft and elastic, a condition which enables them to change their shape as they pass through the smaller capillaries, and to resume their normal shape on entering the larger vessels.

The size of the red blood cells is somewhat variable in different persons. By direct measurement of the cells, Ponder found the greatest thickness to be 2.4 microns, and the least thickness, through the central portion of the cell, to be 1.02 microns. The diameter of the corpuscles varies somewhat according to whether the measurements are made on fresh blood or on dried smears. Using a smear of fresh blood, Ponder and Millar reported a diameter of 8.8 microns, while using stained smears, Price-Jones reported a mean diameter of 7.02 microns (this decrease is due to shrinkage). Some corpuscles, however, exceed these dimensions, while others are smaller. Exceptionally large corpuscles are called *macrocytes*, while the smaller ones are known as *microcytes*.

Erythrocytes are the most numerous of the formed elements of the blood; in the normal adult male they number about 5,000,000 per cubic millimeter; in the adult female about 4,500,000. These figures represent averages, and actual normal counts may vary as much as a million, more or less, from the averages given. In newborn infants the red-cell count is high. Stearns and McKinley give the red-cell count as 5.85 million per cubic millimeter at birth. (This is an estimate based on data taken from the literature.) According to their figures this number drops to a minimum of 3.4 million by the eleventh week and then begins a gradual increase. By the fifteenth week the red-cell count is 4.61 million.

Examined microscopically, red corpuscles appear as homogeneous, structureless corpuscles. Efforts to demonstrate fibrillae or an enveloping membrane have been fruitless. Erythrocytes consist of a fluid or semifluid colloidal material enclosed by a thin protoplasmic membrane, which may differ somewhat in consistency from the rest of the material of the corpuscle. Many investigators have speculated concerning the exact composition of this membrane. At this point we will only mention that it is of a colloidal nature and rich in lipoids. Whatever the nature of this surface layer it is unquestionably the "functional" membrane of the cell. The fluid consistency of the material inside the cell is indicated by the fact that if the membrane is torn, the contents readily flow out. Moreover, parasites which gain access to the cells are able to move about freely.

With certain stains (neutral red or cresyl blue) a delicate reticulum may be observed in some corpuscles. When first observed, this was regarded as constituting a framework by which the shape of the corpuscle was maintained. Later it was thought to be an artifact, due to the precipitation of certain substances in the corpuscles by the reagents which had acted upon it. It has since been shown that these cells are immature red cells *(reticulocytes)* and the reticulated effect is produced by the precipitation of this basophilic protoplasmic substance in the form of granules or filaments. The quantity of this reticulum has been correlated with age of the cell, the younger forms having more of a reticulum. It is not a definite structural entity in the living corpuscle.

Red corpuscles contain about 61 per cent water (by weight), 36 per cent hemoglobin, and the remaining 3 per cent is made up of complex substances in varying amounts. Erythrocytes are composed of *hemoglobin* (a conjugated protein) which gives the blood its red color, and a *stroma.* On analysis, the latter seems to consist of cholesterol, a globulin, and lecithin. The quantities of these constituents vary according to the species of animals.

When erythrocytes are exposed to oxygen, as in the lungs where oxygen tension is high, oxygen and hemoglobin form an unstable combination *(oxyhemoglobin).* In the tissues where the oxygen tension is low, the oxygen is released and the oxyhemoglobin becomes *reduced hemoglobin.* The presence of oxyhemoglobin gives the bright red color to blood in the arteries, while the presence of reduced hemoglobin gives the dark color to venous blood. Using the Van Slyke modification of the Haldane method, it has been possible to determine that 1.34 cc. of oxygen will combine with 1 gram of human hemoglobin. It is likely that hemoglobin is not present in solution in the red corpuscle but exists in the form of a colloidal gel. The amount of hemoglobin present in the blood of men is somewhat higher than for women. The average content for males, 19–30 years of age is 16.21 grams per 100 cc. of blood, and for females 17–30 years of age it is 13.84 grams according to Wintrobe. The hemoglobin values are higher in infants. Stearns and McKinley report an average of 22 grams per 100 cc. at birth. This drops to a minimum between the tenth and twelfth weeks. The amount of hemoglobin then increases gradually, with minor fluctuations, but the normal adult level is not reached and maintained until after puberty.

When red corpuscles are placed in distilled water, the hemoglobin passes from the corpuscles into the surrounding medium. This extraction of the hemoglobin from the red corpuscles is known as *hemolysis*, or "laking" of the blood. The colorless corpuscles which remain after hemolysis are called "blood ghosts." Hemolysis occurs when the osmotic tension of the surrounding medium is low. It may be produced by the action of certain alkalies, acids or by substances called *hemolysins*, which are introduced into or are formed in the tissues.

The plasma is an isotonic fluid normally, that is, an isotonic balance is maintained between it and the corpuscles. Changes in the osmotic tension of the plasma result in changes in the form of the corpuscles. When the solution in which the corpuscles are placed is hypotonic, water passes into the corpuscles which become cup-shaped, or spherical and hemolyzed. When they are placed in hypertonic solutions, water leaves the corpuscles, and they become shrunken with numerous tiny projections appearing on their surfaces (*crenated corpuscles*). In drawn blood and in circulating blood, if it becomes concentrated, the corpuscles form rows by adhering to one another on their flat surfaces. These rows bear a likeness to piles of coins and are known as *rouleaux*.

Substances may be produced by the tissues, under the influence of certain pathological conditions, which cause the corpuscles to collect in clumps or masses. This is known as *agglutination*. The substances which produce this condition are known as agglutinins. Agglutinated masses of corpuscles (thrombi) may cause the obstruction of a blood vessel and shut off the supply of blood to a given area. If this area is one of vital importance, as in the brain or walls of the heart, death is likely to result.

A number of conditions affect the number of red corpuscles in the peripheral circulation. Exercise increases the red-cell count. This increase is due to releasing cells that were stored in the spleen. Change in altitude (higher altitude) causes an increase which is almost immediate (within 20–30 minutes the blood count may increase 2–5 hundred thousand). With the lowered oxygen tension more red corpuscles are necessary to transport the required load of oxygen. Changes in the count occur during menstruation and pregnancy. During and after menstruation, Wintrobe found a decrease in the red-cell count. This may be accounted for by the loss through hemorrhage. Hydremia occurs normally with pregnancy and there is an accompanying slight decrease of erythrocytes. After delivery, however, the count rapidly returns to normal. Climate and temperature have no marked or permanent effect. Sudden temperature changes may produce very temporary effects due to loss of fluid through evaporation (sweating). The most marked change in the number of red corpuscles is that which is produced by pathological conditions.

Conditions lowering the red blood cell count:

1. Hemorrhage--acute or prolonged bleeding.
2. Phenylhydrazine poisoning which causes hemolysis.
3. Exposure to x-rays, etc., which causes bone marrow damage.
4. Various tumor tissues which may invade the bone marrow.
5. Disturbances of the development of the mature red blood cell as seen in pernicious anemia.
6. Hemolysis.
7. Iron deficiency.

Conditions which increase red blood cell count:

1. Various diseases: tuberculosis of the spleen, congenital heart disease (congenital pulmonary stenosis), polycythemia vera, and many others.
2. Drugs and various poisonous substances: nicotine, caffein, arsenic, opium, sodium nitrite, etc., as well as certain of the gases used during war, such as chlorine and phosgene.

The red corpuscles present a number of unusual appearances when they have been acted upon by poisons, or affected by certain pathological conditions. Lead poisoning leads to the precipitation of certain basophilic substances in the corpuscles in the form of granules which give them a "stippled" appearance (*stipple cells*). Other poisons may bring about a disintegration of the hemoglobin, which remains in the corpuscle in the form of small, acidophilic bodies (*Erlich-Heins granules*). Remnants of fragmented nuclei may be retained in the form of one or two sharply defined, granular bodies (*Howell-Jolly bodies*); or the ringlike outline of the nuclear membrane may remain after the nuclear contents have disappeared (*Cabot's rings*). The form of the corpuscle may be altered by assuming a sickle shape, as in sickle-cell anemia.

Leucocytes

The leucocytes or white cells of the blood do not present a constant form, owing to their capacity for ameboid movement, for which reason they belong to the class known as *amorphous cells*. They differ from erythrocytes in being generally larger, in the absence of hemoglobin from their cytoplasm, and in the possession of a nucleus.

The leucocytes are fewer in number than the erythrocytes, averaging about 8,000 to the cubic millimeter. Under varying physiological conditions the number of leucocytes per cubic millimeter may be as low as 6,000 or it may rise to 9,000. When the number falls below or rises above these limits, pathological conditions may be suspected.

Unlike erythrocytes, the leucocytes are functional only to a small extent in the blood stream, their greatest activity taking place in the connective tissues, in which they may be found in considerable numbers. By means of their capacity for ameboid movement they push the cells of the capillary walls apart and enter or leave the capillaries *(diapedesis)*. Thus the blood stream serves mainly as a vehicle for transporting these cells from one place to another where their presence is needed. Nevertheless, although there is some variation in the number of leucocytes present in the blood in different parts of the body, it remains fairly constant for the blood as a whole.

Two classes of leucocytes are generally recognized: *nongranular leucocytes* and *granular leucocytes.* The nongranular leucocytes are characterized by their clear, homogeneous, slightly basophilic cytoplasm; the granular leucocytes (granulocytes) have a cytoplasm which contains numerous, characteristic granular bodies.

NONGRANULAR LEUCOCYTES. Two types of nongranular leucocytes are present in the blood: (1) *lymphocytes* and (2) *mononuclear leucocytes* or *monocytes.*

LYMPHOCYTES. Two sizes of lymphocytes are recognized in the blood, *large* lymphocytes and *small* lymphocytes. Intermediate-sized cells may also be present. Here attention should be called to the fact that the large and small lymphocytes of the circulating blood correspond to the medium and small lymphocytes of lymphatic tissue. The large lymphocyte of lymphatic tissue is found only in the peripheral blood stream under pathological conditions, but it is normally present in the thoracic duct, the right lymph duct and the venous blood of the innominate veins. A most interesting question is, what becomes of these large lymphocytes of the thoracic duct?

The lymphocytes of the blood (measured in dried smears) vary in size from 6–12 microns. The small lymphocytes measuring from 6–8 microns in diameter (being about the size of an erythrocyte), and the large lymphocytes being about 10–12 microns. In fresh blood their size is somewhat smaller. They make up from 20 to 25 per cent of the total white blood cells.

In small lymphocytes the nucleus is so large, relatively, that it fills nearly the entire cell, leaving only a narrow rim of cytoplasm around the outer margin of the nucleus. The amount of cytoplasm is so small in quantity that it is invisible with ordinary magnifications and in ordinary preparations the nucleus is the only part of a small lymphocyte which can be identified. The large lymphocyte differs in having relatively more cytoplasm than the small lymphocyte. The nuclei of both cells usually show an indentation on one side. This indentation is more obvious in the large lymphocyte. The nucleus of the small lymphocyte is filled with a mass of granular chromatin which stains intensely with the basic dyes. The nuclei of the large lymphocytes, due to the finely granular condition of their chromatin, stains somewhat lighter. With the introduction of the use of tissue culture as a means of studying cells, it has been demonstrated that lymphocytes are motile. Their movement is very characteristic. The cell elongates, sends out a process of protoplasm and advances with the nuclear material in the front part of the cell. The cytoplasm of these cells stains a pale blue (basophilic). Dry smears stained by the Romanowsky method show a variable number of azurophilic granules in the cytoplasm of some of the cells. They have been interpreted by some as representing certain phases of cellular activity. These granules are also present in the cytoplasm of monocytes. Not all monocytes, however, contain these azure granules.

In the normal adult, the lymphocytes of the blood develop from the undifferentiated reticular cells in lymphoid tissue (lymph nodes, tonsils, spleen, nodules throughout the alimentary tract, etc.). These reticular cells should not be confused with the histiocyte (phagocytic reticular cell). The lymphocytes then enter the blood stream by passing through the walls of the small venules in their immediate neighborhood. It is not known what their function is in the blood, but they are thought to develop into monocytes and plasma cells. Neither do we know how long they live and circulate. It is believed that large numbers of them leave the body by way of the gastrointestinal tract.

MONOCYTES: (MONONUCLEAR LEUCOCYTES). Monocytes are large cells having an average diameter of 12–15 microns, or even more. They constitute from 3 to 6 per cent of the leucocytes of the blood. The nucleus is located eccentrically in the cell, and is deeply indented or horseshoe-shaped. It is pale in stained preparations, owing to the finely granular character of the chromatin. Their abundant cytoplasm has a slightly basophilic reaction, and may show vacuoles. It is claimed that both mitochondria and a Golgi apparatus are present. With the proper stain, azurophil granules may be seen. The large monocytes show greater activity than the small ones. As they move they send out many pseudopodia of varying sizes and shapes. The origin of monocytes is still being questioned. Some say they are derived from lymphocytes. This claim is based primarily on the fact that there are a number of intermediate forms which can be identified, which link them with the lymphatic series, and which indicate that they are derived from these cells by a process of growth. It may be that they develop directly from the hemocytoblast. It is possible they may have more than one origin. Development of the monocytes takes place, for the most part, in the spleen, liver and bone marrow. Some are formed in the lymphatic tissue and in the loose connective tissue. They function as phagocytes. In areas of inflammation, they leave the blood

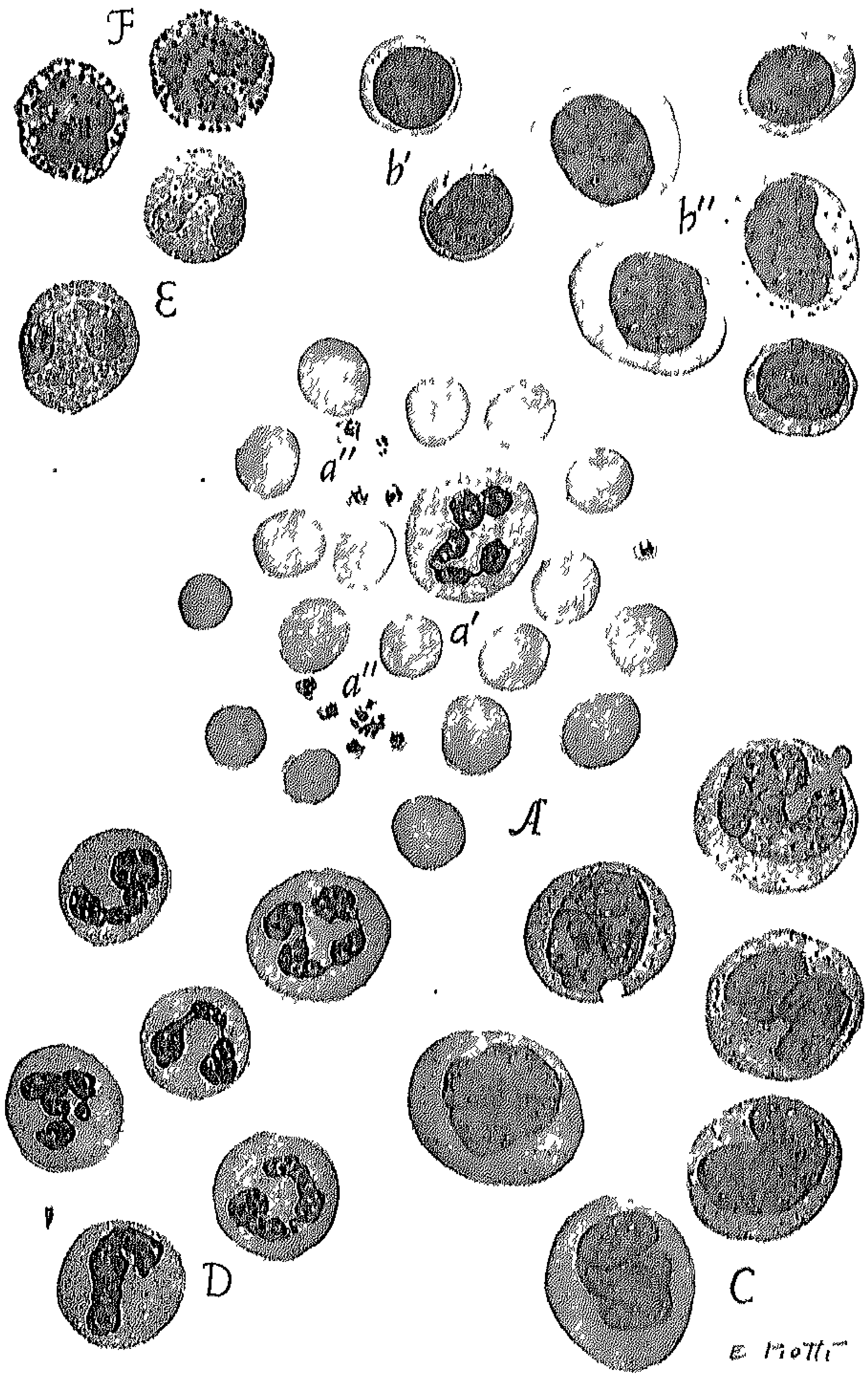


Fig. 19 Cells of normal human blood (smear preparation). (A) Wright's stain, red blood corpuscles; (a′) neutrophilic leucocyte; (a″) blood platelets (B) Lymphocytes; (b′) small lymphocytes; (b″) large lymphocytes. (C) Monocytes; note the difference in the shape of the nuclei; those of the younger cells being less indented than those of the older cells. Granules are present in some of the lymphocytes; also in some of the monocytes (D) Neutrophilic leucocytes. (E) Eosinophilic leucocytes. (F) Basophilic leucocytes (Courtesy, Bremer "Textbook of Histology," Philadelphia, The Blakiston Company.)

stream, migrate into the inflamed tissue and here they hypertrophy and take on the characteristics of macrophages. It is possible that they may develop into fibroblasts or macrophages.

GRANULOCYTES; GRANULAR LEUCOCYTES; POLYMORPHONUCLEAR LEUCOCYTES. The granulocytes are characterized by the possession of a large amount of cytoplasm which is filled with numerous granules. The granules differ in size, in their refractive properties, and in their affinity for the acid or basic dyes, these properties being characteristic for the type of cell in which they appear.

Another characteristic of the granulocytes is the form of the nucleus, which generally presents two or more lobes; the lobes being united by a delicate thread of nuclear material. The lobes may be separated in cells which are, presumably, undergoing degenerative changes. The variety of forms which these nuclei present has led to the use of the term "polymorphonuclear leucocytes," a term which has been shortened by common usage to "polymorphs." After birth these cells arise from the myelocytes of the bone marrow and enter the circulation, by means of their ameboid movement, through the thin walls of the venous sinuses.

Three types of granular leucocytes have been recognized according to the staining properties of their granules. These are the: (1) *neutrophilic leucocytes;* (2) *eosinophilic leucocytes;* and (3) *basophilic leucocytes.*

Neutrophilic Leucocytes: Heterophilic Leucocytes (Neutrophils). Neutrophilic leucocytes are large cells having a diameter of 10–12 microns. These cells are the most numerous of the white cells, constituting from 60 to 70 per cent of the leucocytes of the blood. The cytoplasm itself is homogeneous, but it is filled with fine, closely crowded granules which react to both the acid and basic stains. The result is a characteristic purple, or lilac color (neutral stain). In the younger cells, the cytoplasm stains bluish (basophilic) and the granules are bluish purple. With age, the cytoplasm stains faintly acidophilic and the granules are more reddish purple. The chemical composition of the granules is unknown. Neumann thinks they carry enzymes or enzymelike catalyzers. In young adult cells, the nucleus is band- or rod-shaped but later divides into two or more lobes which are united by fine strands of nuclear material. The network of chromatin threads stains rather deeply. The chromatin is more compact in older cells. There are no nucleoli present in the neutrophils of the peripheral circulation.

The lobation of the nucleus has been the basis for the classification of these cells according to their age. Arneth believed that there was a high correlation between age and number of lobes. On this supposition he devised five classes of cells according to whether the cell has one, two, three, four, or five nuclear segments. The older cells supposedly have the greater number of nuclear segments, however, lobes are not necessarily added one at a time. The Arneth count was used as an indication of bone marrow response to infections, since there is a shift to the more simple nuclear form.

Schilling has devised a simpler method based on this same general idea which has replaced the Arneth count. He divides the cells into a class of unsegmented nuclei ("stab" nuclei) and segmented nuclei.

The neutrophilic leucocytes are very actively ameboid and phagocytic. They have been estimated to move along at the average rate of 34.1 microns per minute at 37° C. They progress by means of pseudopodia, which in these cells are "blunted" projections of cytoplasmic material. Neutrophilic leucocytes are not found abundantly in the tissue spaces under normal conditions, but are confined to the blood stream in which they are, as a rule, phagocytically inactive. When the tissues are invaded by bacteria, or affected by other conditions (inflammations) which result in the destruction of the tissue elements, the neutrophils leave the blood stream and gather in the affected area where they are active in the ingestion of the invading organisms, or fragments of necrotic tissue, which they destroy by a process of intracellular digestion. Because of this activity they are regarded as a "first line of defense" against infections.

Several things may cause a physiological leucocytosis (increased number). There is a daily variation which occurs; before rising in the morning, the leucocyte count is low, by afternoon it has increased as a result of physiological activity. Pain, exercise, mental shock also cause a physiological increase in these cells.

We do not know exactly how long these cells live in the blood, but it is likely their life span amounts to only a few days. They are probably removed from the body, in part, by the phagocytic cells of the liver and spleen. They are also eliminated in the saliva and through the mucosa of the intestine.

EOSINOPHILIC LEUCOCYTES; ACIDOPHILIC LEUCOCYTES (EOSINOPHILS). Eosinophilic leucocytes are practically the same size as the neutrophils, having a diameter of 10–12 microns. They normally make up from 2 to 4 per cent of the white cell count in the adult, but in children it is somewhat higher (6 per cent). According to Domarus, the number is slightly higher in the morning when a person first gets up than during the rest of the day. An eosinophilia is said to exist in the adult if the count goes above 4 per cent.

The nucleus of these cells usually consists of two lobes (rarely three) and stains somewhat lighter than the nuclei of neutrophils. There are no nucleoli. The cytoplasm stains faintly pink and is completely filled with large, highly refractive granules which stain a deep red color with the acid dyes (eosin). Maximow believes these granules are made up of proteins and lipoids. Eosinophils are not vigorously ameboid, their movements are ordinarily slow and the pseudopodia which they form are not extensive. However, they can move as quickly as neutrophils, but only for a short time. Recent findings indicate that these cells may act as phagocytes. The function of these cells is not quite clear; however, they do increase with great rapidity under certain conditions, such as irritating infections of the skin and the invasion of the tissues by parasites and in allergy. They are thought to be related to the metabolism of protein. They are especially abundant in the tissues, bronchi and blood stream in cases of bronchial asthma. They are normally present in many tissues: mucosa of the digestive tract, bone marrow, lymphoid organs, and are numerous in the lactating breast. The eosinophils of the blood and those of the connective tissues are identical.

Basophilic Leucocytes (Basophils). Morphogenically there are two types of basophilic cells in the body: the basophilic leucocytes of the blood and the basophilic cells of the tissues (mast cell). These two cells have only one thing in common, that is their basophilic staining granules. In mammals the mast cell of the connective tissues may arise from several sources; the basophilic leucocyte, however, is derived from the myeloid elements of the bone marrow.

The basophilic leucocytes are somewhat smaller than the other granulocytes, their diameter varying from 8–10 microns. They are the least numerous of the granulocytes, constituting from 0.5 to 1 per cent of the total number of the leucocytes of the blood. They are not actively ameboid, but move about more slowly than either of the other granulocytes. The nucleus is polymorphous, consisting of three, rarely more, relatively large lobes. In stained material the nuclei are pale (the chromatin network is loosely arranged) and may be almost completely obscured by the deeply stained granules which fill the cytoplasm. The cytoplasm is homogeneous and stains faintly acidophilic. Irregularly scattered through the cytoplasm are a number of highly refractive round granules of variable size, which stain intensely with the basic dyes. These granules are water soluble and with ordinary staining procedures are usually partially or completely destroyed. While it has been believed rather generally that these cells are not phagocytic, both Betances and Ringogen report them capable of phagocytic activity. The function of these cells is not known, but their reactions in response to certain pathological conditions have been observed and are of interest. During acute inflammatory reactions and in infectious diseases they disappear from the blood stream. They may be increased in polycythemia, myelogenous leukemia, tuberculosis and cirrhosis of the liver. A decrease in the number of basophils takes place after the injection of adrenalin and thyroxin, and after infection with syphilis.

BLOOD PLATELETS: THROMBOCYTES

Blood platelets are small, non-nucleated masses of protoplasm one-half, or less, the size of an erythrocyte (2-4 microns). Their number averages about 250,000 per cubic millimeter. Blood platelets are produced by giant cells *(megakaryocytes)* in the bone marrow. The megakaryocytes extend long pseudopodia into the capillaries by pushing aside the cells of the capillary walls. The ends of these pseudopodia are constricted off and float away in the blood stream to become blood platelets. They are round or oval, but are frequently found presenting an irregular (stellate) outline. They consist of a clear, hyaline, outer protoplasm *(hyalomere)* which encloses a granular, chromatic portion *(chromomere)*. This inner granular core has been mistaken for a nucleus.

The theory of the process of blood clotting may be given in the following manner:

1. Prothrombin + thromboplastin + calcium = thrombin
2. Thrombin + fibrinogen = fibrin.

The exact mechanism involved in the first step in blood clotting is still a controversial point, so the following discussion is based on Howell's interpretation of the process. Thrombocytes are functionally related to the clotting of blood and whenever clotting occurs clusters of these thrombocytes appear with threads of fibrin extending from them. A substance, antiprothrombin, is present as a normal constituent of the blood. Ordinarily it exists in combination with prothrombin thus preventing the formation of clots in the circulating blood. When the blood is exposed by injury to the vessels, or by other means, the thrombocytes and the damaged tissue cells are believed to release the substance, thromboplastin, which combines with or neutralizes the antiprothrombin. The prothrombin thus released from the antiprothrombin is free to react with the calcium to form thrombin. The thrombin reacts with fibrinogen of the blood and the latter is precipitated in the form of fibrin threads, thus forming the stroma of the clot. The inability of the thrombocytes to release a sufficient amount of the thromboplastin is regarded as a factor in the condition known as hemophilia, in which the blood continues to flow without clotting, even when the extent of the injury is slight.

During the day there is a slight physiological change in the number of platelets. Both hunger and severe exercise cause an increase in their number and a marked increase occurs after most operations. Before the onset of menstruation, the number of platelets decreases. Pregnancy also affects the platelet number. During the course of pregnancy there is a gradual increase which becomes accelerated toward the end of pregnancy, and during labor the number decreases, but rises again after the end of labor.

HEMOCONIA

Hemoconia (sometimes called blood dust) are small, vibrating particles found in the plasma. Their exact nature is not known. They are about as large as the granules in granular leucocytes and it has been suggested that they may be extruded granules, but there is no adequate proof of this. Another suggestion is that they are the particles of disintegrating red blood cells. It is of interest that the number of these hemoconia is greatly increased in chronic myeloid leukemia and that they decrease in number in aplastic anemia.

CHYLOMICRONS

Other bodies which occur in the blood are small globules of fat, called *chylomicrons,* which are especially abundant after a meal in which a considerable quantity of fat is present.

LYMPH

Lymph is a colorless fluid which is contained in a series of vessels, the *lymphatics.* Although the lymphatics communicate eventually with the blood vessels, the lymph differs in several respects from the blood, having a lighter specific gravity, and containing no red corpuscles, platelets or fibrinogen. On the other hand, it contains numerous lymphocytes and a few granulocytes. It also coagulates, but quite slowly. It appears to be intermediate between the tissue fluids and the blood. Unlike the blood it does not carry oxygen, but may contain considerable quantities of carbon dioxide. Digested fats are transferred to lymphatics *(lacteals)* in the wall of the intestine, giving the lymph a milky appearance *(chyle).*

THEORIES OF THE ORIGIN OF BLOOD CORPUSCLES

During the entire life of the individual new blood cells are being formed to replace the cells of the peripheral circulation that are dying or being destroyed. In the adult the lymphocytes and monocytes develop in lymphoid tissues and for this reason are called *lymphoid elements.* The remaining blood elements (erythrocytes, granulocytes and blood platelets) develop normally in the red marrow of the bones; this is myeloid tissue and the cells developed there are called the *myeloid elements.* Certain pathological processes in the adult may interfere with the normal development of blood cells in the bone marrow, and under these circumstances it is possible for the spleen, lymph nodes and liver to again take over the function of forming blood cells (*hemopoiesis*). This type of blood formation is known as *extramedullary hemopoiesis (extramedullary myelopoiesis).*

Although a great deal of attention has been given to the origin of the formed elements of the blood, the different interpretations of the results of these studies have led to a confusion of ideas by which the subject is still greatly obscured. The point around which the controversy occurs is whether, after birth, all cells of the blood originate from a common stem form, or whether more than one stem cell form exists. As a result of this disagreement two main schools of thought have developed. One, the *monophyletic (unitarian)*, which is supported by Pappenheim and Maximow, and which is adhered to in this text, has a single stem cell with polyvalent potentialities. This cell is designated as a "lymphoidocyte" or "hematocytoblast." It is a constituent of all adult hemopoietic tissue and from this stem cell are said to be derived all of the blood cells. The second group, the *polyphyletics,* refuse to recognize this cell as the progenitor of all blood cells, but in turn they fail to agree among themselves as to whether there are two or three stem cells present from which the blood cells arise. Because of this they have formed two groups within the "polyphyletic" ranks. The *dualists,* represented by Ehrlich, Naegeli and Piney, believe that there are two stem cells giving rise to the blood cells. The granulocytes and monocytes arise from a common stem cell, the myeloblast, while the lymphoblast gives rise to the lymphocytes. They fail, however, to agree concerning the origin of the red blood corpuscles. According to Naegeli, the erythroblast is derived directly from the myeloblast. Piney thinks the erythroblast develops from the reticulo-endothelial cells. Sabin and her colleagues (the *trialists),* believe there are three stem cells (derived from primitive free cells, which in turn were formed from undifferentiated reticular cells), one for each of the types of blood cells. The myeloblast of the bone marrow is the progenitor of the granular cells, the lymphoblast of lymphoid tissue is the parent cell of the lymphocytes, while the monocytes stem from monoblasts of connective tissue. According to Sabin, et al., the red blood corpuscles originate from reticulo-endothelial cells lining the blood vessels of the bone marrow.

CELLS IN BONE MARROW AND THEIR DEVELOPMENT

IMMATURE CELLS IN BONE MARROW

The immature cells in bone marrow are those which represent the different stages through which the mature cells have passed. The first formed elements of the blood arise, in the embryo, from the primitive mesenchyme. The cells of reticular tissue retain the characteristics of mesenchymal cells, and are more nearly like them than those of any other tissue of the adult body. This is especially true of the tissue which forms the framework of the lymphoid organs and of the bone marrow. Not only do the reticular cells possess marked phagocytic properties (see reticulo-endothelial system, p. 58), but they are able to free themselves from the reticulum and undergo extensive changes.

MATURE CELLS IN BONE MARROW

The mature cells which are present in bone marrow, with the exception of certain forms to be described later, are *lymphocytes, monocytes, granulocytes (neutrophils, eosinophils,* and *basophils)* and *erythrocytes.* These cells are similar in all respects to those found in the blood stream. They are intermingled in the marrow with the other myeloid elements, and are to be regarded as a reserve supply, ready to enter the blood stream as they are needed.

LYMPHOCYTES. In the lymph glands and other lymphoid organs undifferentiated reticular cells give rise to the large and medium lym-

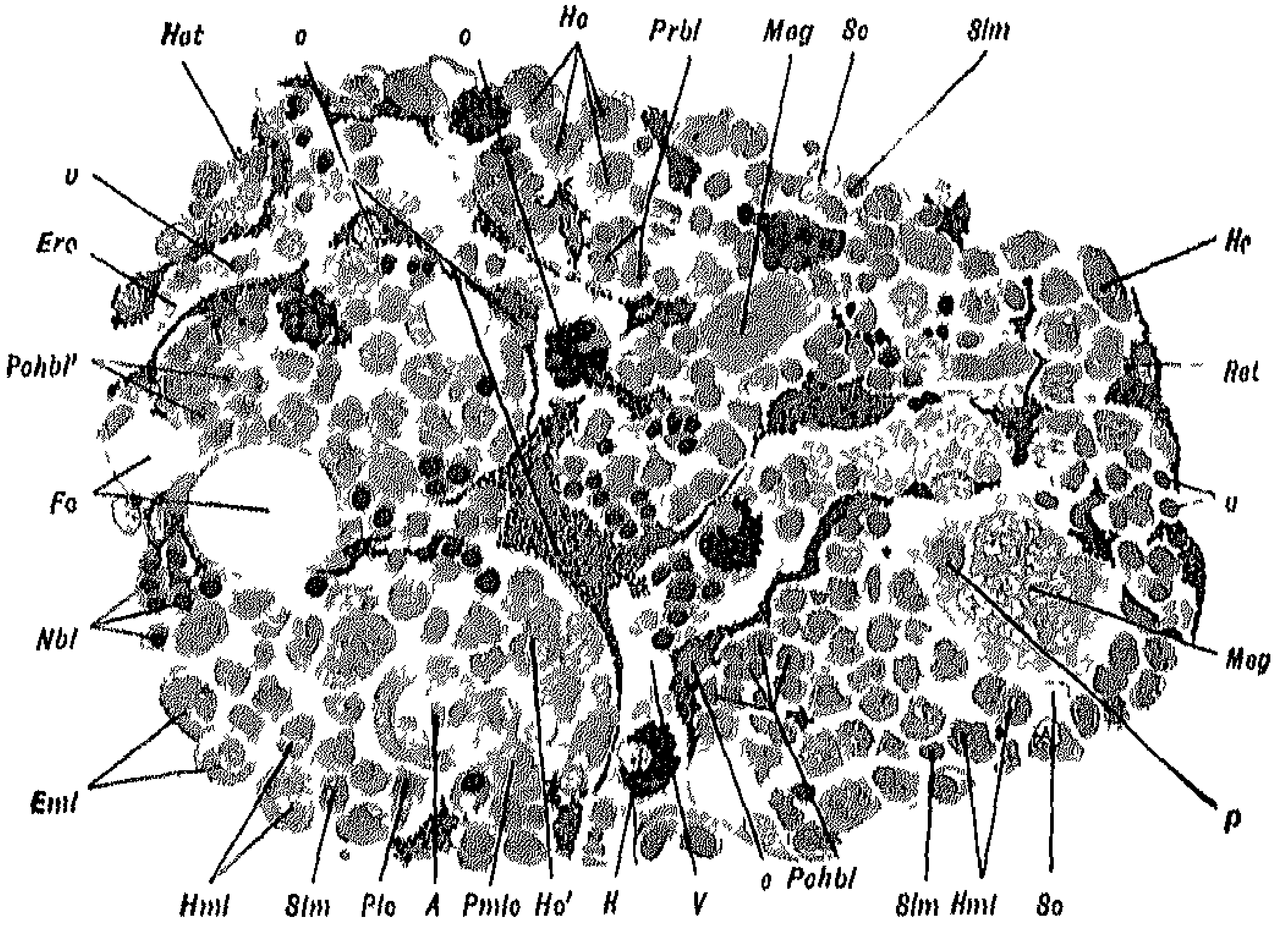


FIG. 50. Section of bone marrow of a rabbit (from Maximow). *(A)* Artery. *(Ret)* Reticular cells. *(Hc')* Hemocytoblast in mitosis. *(Slm)* Small lymphocyte. *(Meg)* Megakaryocyte with ingested neutrophilic leucocyte. *(Prbl* and *Pchbl)* Proerythroblasts. *(Pchbl')* Proerythroblasts in mitosis. *(Pmlc)* Promyelocytes. *(Plc)* Plasma cells. *(Hml)* Heterophil myelocytes. *(Eml)* Eosinophil myelocytes. *(Erc)* Erythrocytes. (Courtesy, Maximow and Bloom: "Textbook of Histology," Philadelphia, W. B. Saunders Co.)

phocytes of lymphoid tissue. Their cytoplasm is basophilic, the nuclei stain rather lightly and contain usually one or more nucleoli. These cells multiply by mitosis, in the germinal center of the lymph nodules and throughout the lymphoid tissue. The products of this division are the small lymphocytes, which then enter the circulation, either by penetrating the capillary walls of the blood vessels in the immediate neighborhood or entering the lymphatic vessels first and then reaching the blood circulatory system.

The advocates of the "unitarian" theory believe the primitive cells of the bone marrow and the larger lymphocytes are identical, merely differing in their location. According to them, these cells form the common stem cell or *hemocytoblast* which has the potentialities of differentiating into the various blood cells. Moreover, they believe that lymphocytes have the capacity of reassuming mesenchymal potentialities. The "dualists," however, claim that the primitive cells of the marrow are not the same as the large lymphocytes. They call these large lymphocytes, *lymphoblasts*, and believe they give rise only to cells of the lymphoid series, of which the small lymphocyte is the final stage.

MONOCYTES. Many investigators (unitarians) believe that lymphocytes may develop into monocytes. They base their conclusion on the presence of transitional forms between lymphocytes and monocytes, which makes it very difficult to differentiate between the two. They also believe that the monocyte develops directly from hemocytoblasts.

Several other origins are given for monocytes. Mallory, Foot, Hess and others describe the monocytes as developing from endothelium. Aschoff and Kiyono say they develop from histiocytes, while Sabin and her colleagues give the monoblast as the parent cell.

The monocytes are actively phagocytic and are highly specialized, since they seem to be, with few exceptions, incapable of further division. A small number of lymphocytes and monocytes are present in bone marrow, where, in all probability, they have their origin. The greater number of the cells of the lymphatic series, however, originate in the lymphoid organs, for which reason they are referred to as *lymphoid elements.*

BLOOD CELLS OF THE MYELOID SERIES

The cells whose origin is restricted to the bone marrow constitute the *myeloid elements* of the blood. They are principally the erythrocytes and the granular leucocytes. Another constituent of myeloid tissue is the megakaryocyte which is supposed to give rise to blood platelets. A few lymphocytes and monocytes are also found in this tissue. There is considerable evidence to support the belief that, when certain pathological conditions interfere with the formation of these elements in the marrow, they may be formed in the spleen and lymph glands. The formation of erythrocytes in the lymph glands, under these conditions, is fairly well established.

The first progenitors of the erythrocytes and granulocytes in the bone marrow are derived from the reticular cells. These cells separate themselves from the reticulum, but remain in the marrow. Their cytoplasm becomes strongly basophilic and may be vacuolated. There are no specific granules but once in a while azurophilic granules may be seen. Their nuclei enlarge, the chromatin forming a delicate reticulum. Two, or more, deeply staining nucleoli are frequently present. They have a diameter of 15 microns, or more. These cells are the *hemocytoblasts (myeloblasts* in clinical literature), or the stem cells from which the erythrocytes and granulocytes of the blood stream are derived.

GRANULOCYTES. The order of development of granulocytes is: reticular cells → hemocytoblasts (myeloblasts) → promyelocytes → myelocytes → metamyelocytes → and granular leucocytes.

The hemocytoblasts are transformed directly into *promyelocytes* which are cells with a somewhat less basophilic cytoplasm. A few granules make their appearance in the cytoplasm in the region of the nucleus. According to the staining properties of their granules, these cells are known as *neutrophilic, eosinophilic,* or *basophilic promyelocytes.* Since these changes take place rather rapidly, only a relatively small number of hemocytoblasts are to be found in adult bone marrow.

The promyelocytes divide rapidly; the cells formed by these divisions becoming *myelocytes,* which are the most numerous of the cells of the bone marrow. Myelocytes are to be distinguished from promyelocytes by their somewhat smaller size, a reduction of the basophilia of their cytoplasm, and an increase in the number of granules which the cytoplasm contains. The greatest increase in the number of cells in the marrow is due to the mitotic divisions of the myelocytes. After an unknown number of generations of these cells have been produced, their nuclei undergo transformation which point to their future lobulation. The cells in which these nuclear changes can be observed are known as *metamyelocytes.* Through a still further reduction of the basophilia of their cytoplasm an increase in the number of the granules and the assumption of a horseshoe-shaped nuclei, the metamyelocytes are transformed, according to the character of their granules, into *neutrophilic, eosinophilic* and *basophilic leucocytes.*

ERYTHROCYTES. The erythrocytes also originate from the hemocytoblasts and pass through a somewhat similar series of transformations: hemocytoblasts (myeloblasts) → proerythroblasts → erythroblasts → normoblasts → reticulocytes → and erythrocytes.

Hemocytoblasts become proerythroblasts (megaloblasts) with the appearance of a small amount of hemoglobin in their cytoplasm. These cells are large, with large nuclei. The chromatin is rather scant and has a delicate meshwork arrangement. The nuclei contain well-defined nucleoli.

In the proerythroblast only a small amount of hemoglobin is present and the cytoplasm is predominantly basophilic. The proerythroblasts divide mitotically to become erythroblasts.

Erythroblasts are to be identified by a considerable increase in the amount of hemoglobin in their cytoplasm and by nuclei in which the coarse masses of chromatin assume what is known as a "checker-board" arrangement. These cells are somewhat smaller than the proerythroblast. The increase in the amount of hemoglobin in the cytoplasm of the erythroblasts (many generations are present, and in each succeeding generation the amount of hemoglobin is increased) results in a variety of colors in these cells, when the usual blood stains are employed. These may range from the blue of the earlier generations to purple or lilac in the later generations. Owing to the diversity of colors which may be observed in these cells, they are said to be *polychromatophilic*. The erythroblasts undergo repeated divisions and become smaller. There is an increase in the hemoglobin content of their cytoplasm, to the extent that it gives the acidophilic reaction of mature corpuscles in stained smears. These cells are now known as *normoblasts*.

In the younger forms of the normoblasts the nuclei are relatively large and appear reticular, while in the older cells they are smaller and the chromatin is dense and stains deeply. The number of normoblasts also increases by division, the nuclei in each generation of these cells becoming smaller and more deeply staining. This continues until the nuclei are shrunken and pyknotic, after which division of the cells ceases. Finally the nucleus is extruded from the cell, and the normoblast becomes a reticulocyte or young erythrocyte.

Reticulocytes are similar in appearance to the erythrocyte of the peripheral circulation, except that they contain a delicate reticulum in their cytoplasm which can be seen only if the cells are stained with some supravital stain such as cresyl blue. These cells are usually restricted to the bone marrow, only a few of them (0.5 to 1 per cent of erythrocytes in peripheral blood) escaping into the peripheral circulation. With the loss of the reticulum, the reticulocytes become the mature erythrocytes of the blood stream.

Various views are held regarding the manner in which the nucleus of the normoblast is disposed. One conception is that the nucleus is fragmented and resolved into the substance of the corpuscle. In some cases these fragments are said to persist as the Howell-Jolly bodies. Others hold that the nuclear substance is dissolved in the stroma of the corpuscle, the nuclear membranes sometimes remaining as the Cabot rings. The general belief is that, whether or not the nucleus is fragmented, it is extruded from the body of the corpuscle. The presence of nuclei among groups of erythrocytes in the bone marrow strongly supports this view.

MEGAKARYOCYTES. Megakaryocytes are giant cells which are found in the bone marrow, and which may appear in the blood stream at times. Their abundant cytoplasm is clear and homogeneous. The large nucleus is divided into a number of irregular lobules, and is frequently horseshoe- or ring-shaped. Numerous centrioles may be demonstrated, and mitochondria and a Golgi apparatus have been described. These cells are usually irregular in form owing to their capacity for ameboid movement.

After a time, megakaryocytes undergo degenerative changes. In this condition they may enter the blood stream and are carried to the lungs, in the capillaries of which they are destroyed by autolysis. It is reported that blood platelets are more numerous in the lungs than elsewhere in the body. Under pathological conditions unmodified, as well as modified, megakaryocytes may enter the blood stream and become so numerous in the capillaries of the lungs as to obstruct the flow of the blood.

Megakaryocytes are formed by an increase in the amount of the cytoplasm, and hypertrophy of the nuclei of the hemocytoblasts. Constrictions are formed in the nuclei as if they were about to divide. These constrictions, however, do not deepen to the point of division, but, instead, give the nuclei their irregularly lobulated appearance.

SUMMARY

COMPOSITION: 1. Cellular elements
- a. Red blood corpuscles
- b. White blood cells
- c. Thymocytes or platelets

2. Fluid matrix (plasma)
3. Potential fibrous elements (fibrin)

QUANTITY: Volume of blood in the body has been estimated (using the dye method) to be about one-twelfth the body weight. In the average adult this amounts to approximately 6,000 cc.

Cellular elements of the blood:
- a. Erythrocytes (red blood corpuscles)
- b. Leucocytes (white blood cells)
  - (1) Nongranular
    - (a) Lymphocytes
    - (b) Monocytes
  - (2) Granular
    - (a) Neutrophils
    - (b) Eosinophils
    - (c) Basophils
  - (3) Thymocytes or platelets

CHARACTERISTICS OF THE CELLULAR CONSTITUENTS OF THE PERIPHERAL CIRCULATION

Name	*Number per Cubic Millimeter*	*Diameter in Micra*	*Percentage*	*Nucleus*
1. Erythrocytes	5,000,000 male 4,500,000 female 5,850,000 newborn	7–8		
2. Leucocytes	6,000-9,000	Variable		
Nongranular				
Lymphocytes		6–12	20–25	Relatively large, round or indented on one side Stains deeply
Monocytes		12–15	3–6	Indented or horseshoe shaped Lightly staining
Granular				
Neutrophils		10–12	60–70	Band-shaped in young cells Polymorphonuclear in older cells
Eosinophils		10–12	2–4	Usually bi-lobed Stain lightly
Basophils		8–10	0.5–1.0	Polymorphous, usually 3 lobes Stains rather lightly
3. Thrombocytes	250,000	2–4		No nucleus

CHARACTERISTICS OF THE CELLULAR CONSTITUENTS OF THE PERIPHERAL CIRCULATION

Name	*Cytoplasmic Granules*	*Derivation of Cell*	*Differential Potentialities*	*Motile*	*Phagocytic Capabilities*
1. Erythrocytes					
2. Leucocytes					
Nongranular					
Lymphocytes	Small azurophilic granules usually present	Undifferentiated reticular cell of lymphoid tissue	Monocytes Plasma cells	Yes	None or very slight
Monocytes	May have few, small azurophilic granules	Lymphocytes according to some Monoblasts according to others	Fibroblasts Macrophages	Yes	Marked
Granular					
Neutrophils	Numerous fine, uniform neutrophilic granules	Bone marrow	None	Yes	Marked
Eosinophils	Many large, uniform, red-staining (eosinophilic) granules	Bone marrow	None	Yes	Slight
Basophils	Many large, irregularly sized, blue-black (basophilic) granules	Bone marrow	None	Slightly or not at all	None or very slight
3. Thrombocytes	Inner granular core	Megakaryocytes of bone marrow	None	No	None

White blood cells differ from red blood corpuscles as follows:

a. Are generally larger than red blood corpuscles
b. Contain no hemoglobin
c. Possess a nucleus

PLASMA: It is a fluid that contains albumin, globulin and inorganic salts. It is slightly alkaline, feels "soapy" and has a yellowish color.

SERUM: is blood minus fibrin and the formed elements. It appears as a thin yellowish fluid.

HEMOCONIA (BLOOD DUST): are small, vibrating granular particles found in the plasma. Exact nature or function of these particles is unknown.

CHYLOMICRONS: Small globules of fat which occur in the blood, particularly abundant after a fatty meal.

LYMPH: A colorless fluid, containing numerous lymphocytes and a few granulocytes, which flows in lymph vessels. It has a lighter specific gravity than blood, and contains no red corpuscles, platelets or fibrinogen.

8

Muscular Tissues

The muscles are the contractile tissues of the body. Three kinds of muscle tissue are recognized on the basis of certain structural and functional differences: *smooth* or *nonstriated, striated* or *skeletal,* and *cardiac muscle.* The individual has no control over the contraction of smooth muscle, hence this type of muscle is said to be *involuntary.* Striated muscle is spoken of as *voluntary* muscle because, for the most part, its movements are the result of volitional impulses. Cardiac muscle, being independent of the will, but having striations, is called *striated involuntary* muscle.

SMOOTH MUSCLE

Smooth muscle consists of spindle-shaped (fusiform) fibers, with the nucleus occupying the center of the fiber in its thickest part. Usually the fibers are arranged in layers or sheets, with the fibers parallel to one another, as in the walls of blood vessels. They may also be arranged in bundles in which the fibers are parallel, but with the bundles themselves forming layers which lie in different directions. This arrangement is seen in the wall of the intestine, the wall of the urinary bladder and in the uterus. The fibers may occur singly, or in small bundles, in association with certain structures such as the hair follicles.

Smooth muscle, except for that found in the muscle of the iris of the eye and the arrectores pilorum (muscle to the hair) which is derived from ectoderm, is developed from mesenchyme (mesoderm). In the embryo, myoblasts develop by differentiation from the mesenchymal elements. Later, already differentiated myoblasts divide to form new myoblasts. Formation of new muscle fibers does not occur in the adult, with two possible exceptions: the uterus during pregnancy, and muscle cells in relation to vascular buds in wound healing. In the former case it is believed that under the stimulus of the female sex hormones (as demonstrated in rabbits) smooth muscle cells undergo mitosis and hyperplasia, or undifferentiated cells may form new muscle cells. In the latter situation the new muscle fibers of the young vascular sprouts are thought to arise from primitive perivascular cells.

The fibers of smooth muscle vary considerably in size. In the walls of the smaller arteries they may be only 0.015 0.02 mm. in length (15–20 microns). The average length of the fibers in the wall of the intestine is 0.2 mm. In the pregnant uterus smooth muscle fibers may attain a length of 0.5 mm. or more (approximately 500 microns). Fibers vary in width from 3 8 microns.

Owing to their closeness to one another and the manner in which they overlap, it is extremely difficult to observe the form of the fibers in longitudinal sections of smooth muscle. They are usually arranged so that the thin portion of one fiber lies on the thick portion of another. When separated from one another, as in teased preparations, each fiber is seen to be an elongated structure which is thickest in its middle portion, from which it tapers more or less gradually according to its length, to its tapered ends. An oval or rod-shaped nucleus is located in the central portion of the fiber in its thickest part. The nucleus contains a number of small chromatin granules and is surrounded by a mass of granular protoplasm. When the fiber is in the contracted condition, the nucleus may appear to be bent or twisted.

When viewed with the higher powers of the microscope, the fibers

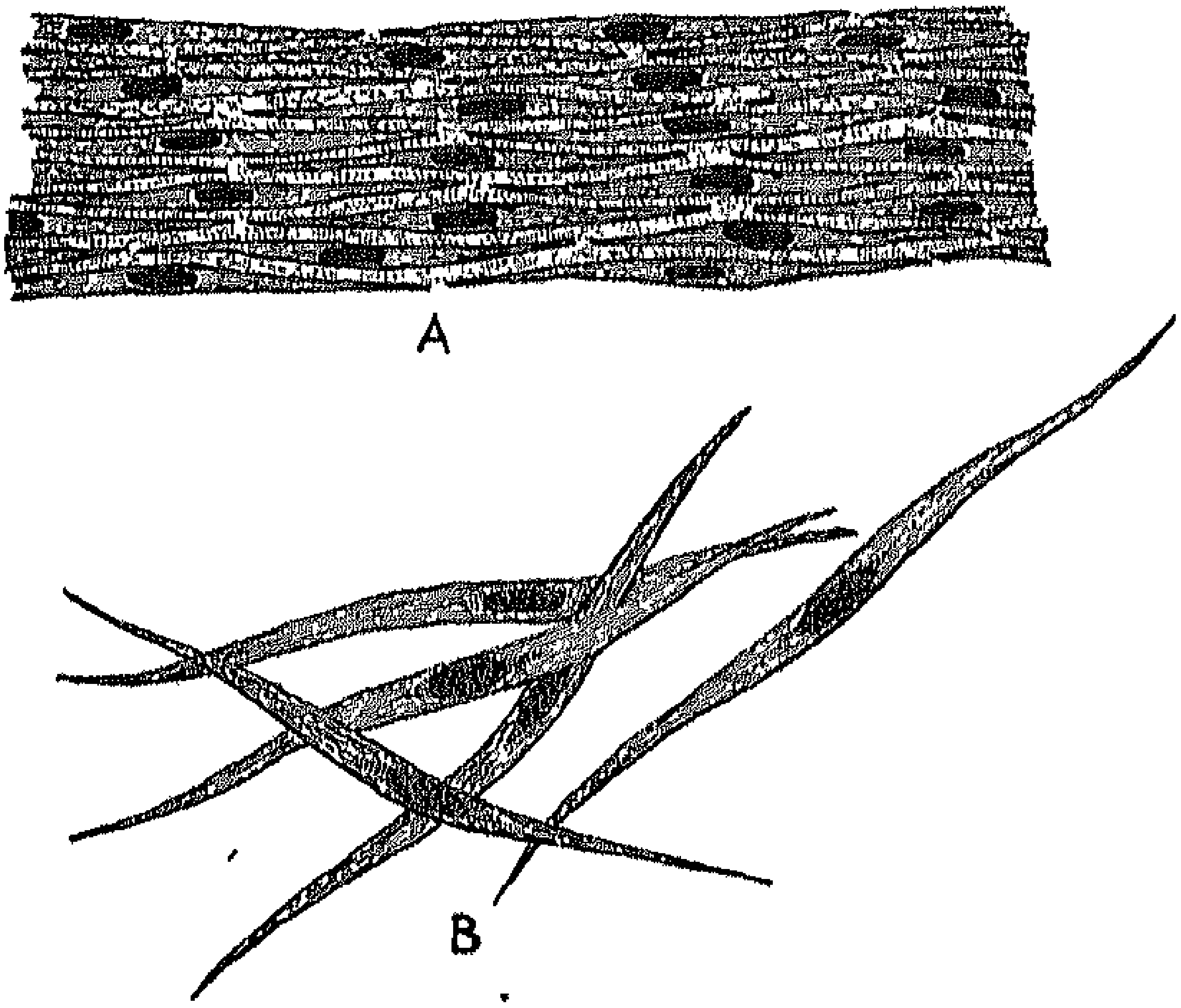


FIG. 51. Smooth muscle fibers (A) Cells of smooth muscle tissue from the wall of the intestine (B) Smooth muscle cells from teased uterine muscle.

present a faint longitudinally striated appearance. This is due to the presence of a number of delicate fibrillae *(myofibrillae)* which extend from one end of the fiber to the other. The fibrillae are regarded as the contractile elements of the fiber. A number of stiff protoplasmic fibrils which lie outside the myofibrillae are known as *border fibrils (myoglia).* The border fibrils can be demonstrated by the use of special stains (Mallory's phosphotungstic acid hematoxylin) and can be seen in some cases to pass from one fiber to another.

The myofibrillae are surrounded by a fluid protoplasmic substance *(sarcoplasm)* which fills the body of the fiber. The granular cytoplasm surrounding the nucleus is an undifferentiated form; the myofibrillae and sarcoplasm being differentiated forms of protoplasm. The protoplasm at the surface of the fiber is still further differentiated and forms a thin membrane *(plasma membrane)* by which the substance of the fiber is invested. The myofibrillae have the same structure throughout and are not marked by alternate light and dark bands as in striated muscle.

In transverse sections of smooth muscle, the fibers are large and round where the section is through their thicker portions, but become smaller and more irregular in size as the section passes through the portions nearer the ends. Where the nuclei appear in transverse sections they are seen to occupy the center of the fiber. In properly prepared sections the myofibrillae appear as minute bright dots arranged around the nucleus.

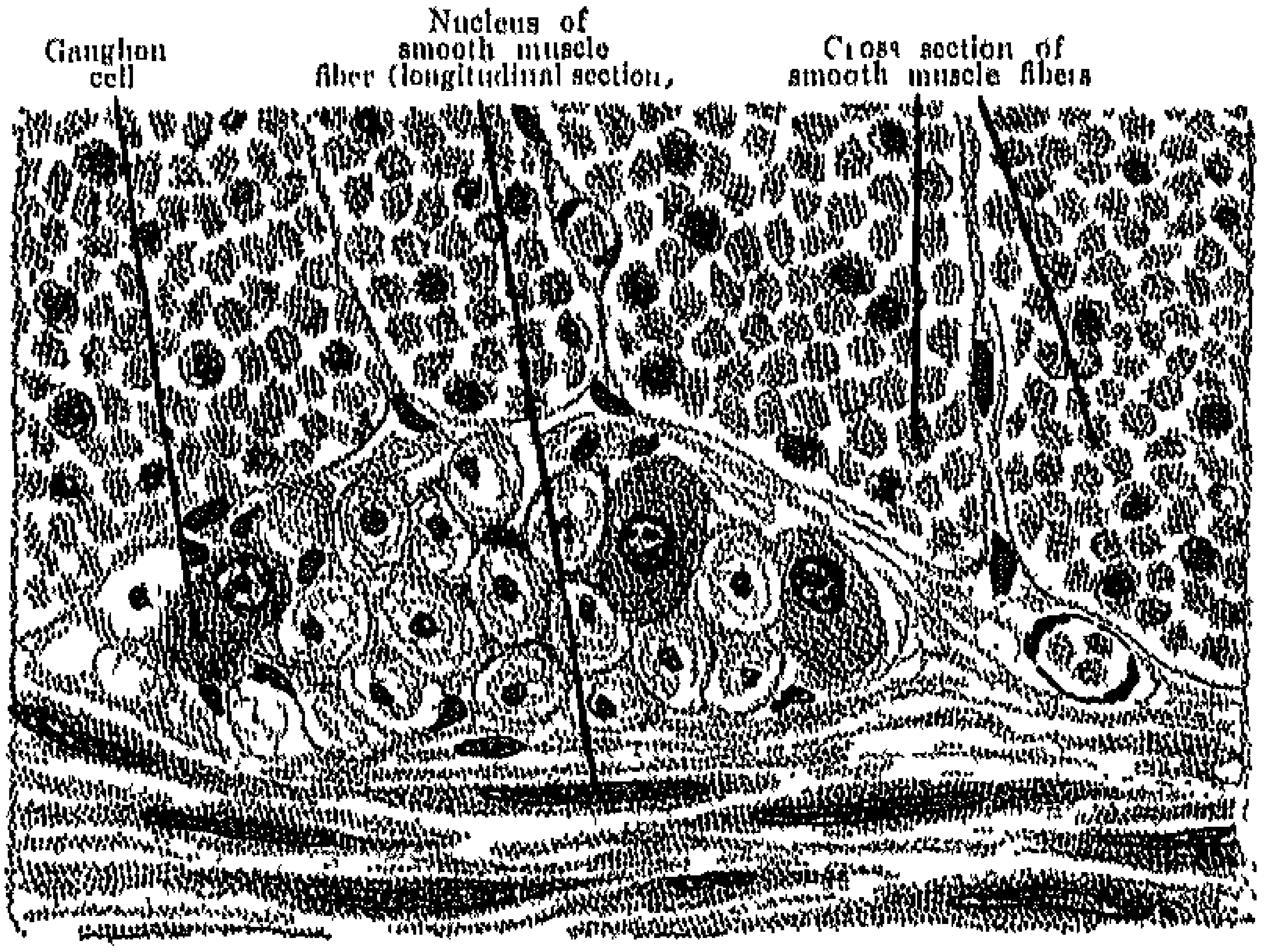

Ganglion cell
Nucleus of smooth muscle fiber (longitudinal section)
Cross section of smooth muscle fibers

FIG. 52. Cross and longitudinal sections of smooth muscle. A nerve plexus is shown between the two layers of muscle.

Opinions differ regarding the manner in which the fibers are attached to one another in the tissue. One view is that they are made to adhere to one another by a cement substance which is applied to their surfaces. Another view is that they are attached by protoplasmic bridges which pass from fiber to fiber, in which case smooth muscle would form a syncytium. As has been indicated, the border fibrils may pass from one fiber to another, but whether this represents a syncytial condition is questionable. In preparations which have been stained with selective dyes, delicate reticular and elastic fibers can be demonstrated around the individual fibers of smooth muscle. Binding the fibers together in bundles are thin layers of collagenous and elastic tissues.

In stained longitudinal sections of smooth muscle, irregular, deeply stained bands are frequently seen crossing the fibers. These bands indicate areas of contraction in the muscle.

There are two ways in which smooth muscle fibers may contract: as a whole fiber shortening uniformly throughout its entire length, or a wavelike contraction may proceed throughout the length of a single fiber. In sheets of smooth muscle, if this wave-type contraction occurs, it proceeds in a more or less straight line across a number of fibers and therefore the contraction area of one cell may be at its extremity, while the adjacent cell shows this area near its central part. *In smooth muscle the contraction is slow and sustained, in marked* contrast to the rapid, short type of contraction of striated muscle.

Although smooth muscle is richly supplied with blood, it is not as vascular as either striated or cardiac muscle. The larger vessels are located in the broader septa, their branches extending into the smaller septa between the muscle bundles or layers, where they subdivide and form capillaries which are arranged in a network about the smaller bundles of muscle fibers rather than about single fibers.

The nerves are branches of the sympathetic system which accompany the blood vessels in the septa. There is no direct evidence that these nerves end in relation to every individual muscle fiber. It has been suggested rather that the syncytial arrangement of the tissue with its protoplasmic continuity allows for the progression of the impulse, or that along a line of contraction the cells pull neighboring cells and this mechanical stimulus effects the spread of the contraction wave.

Smooth muscle is the contractile element present in all organs or structures where muscle is present and not under voluntary control. It is found in the walls of blood vessels and the larger lymphatic vessels, the walls of the digestive tract from the middle of the esophagus to the anus, in the gall-bladder, ureter, bladder and urethra, posterior wall of the trachea and the bronchial tree, in the lymph glands and the spleen, testes, prostate, the ducts of the male generative system, corpora cavernosa of the penis, broad ligament, uterine tube, uterus and vagina. It forms the arrectores pilorum of the hair, and the muscle of the ciliary body and iris of the eye.

STRIATED MUSCLE

✓ Striated or skeletal muscle differs from smooth muscle in the size and shape of its fibers, the arrangement of the fibrillae, the number and position of its nuclei, and in having its substance enclosed by a definite membrane, the *sarcolemma*. The fibers are also crossed by alternate light and dark bands which give them a "striated" or "striped" appearance.

Striated fibers are bound together in bundles or *fasciculi*. The fibers are bound together to form *primary bundles* which are separated by thin sheets or septa of connective tissue. A number of primary bundles are invested by somewhat broader connective tissue septa to form *secondary bundles* which, in turn, are grouped to form *tertiary bundles*. The entire muscle is invested by a connective tissue sheath, the *epimysium*. The septa which lie between the muscle bundles or fasciculi are extensions of the connective tissue of the epimysium and constitute the *perimysium*. The *endomysium* consists of a delicate network of reticular connective tissue which extends from the perimysium into the bundles and envelops the individual muscle fibers.

Striated fibers are cylindrical or slightly flattened cylindrical structures having conical or tapering ends. They vary in length from 1 mm. (in the smallest muscles) to 4.5 mm. (in the largest muscles) according to the size of the muscle and the length of the fasciculi in which they occur. The fibers vary from 10–100 microns in diameter, but within a particular muscle the size of the individual fibers is approximately the same diameter. However, the size of the fibers seems to correlate quite well with the size of the muscle (i.e., large muscles, such as the gluteus maximus, will have fibers of large diameter, while the smaller muscles, such as the ocular muscles, will have fibers of smaller diameter). The diameter of the fibers of a muscle will increase with prolonged exercise or work and will decrease if the muscle is immobilized for a period of time, even though the muscle is uninjured and is healthy tissue.

Each fiber consists of a fluid protoplasmic substance, the *sarcoplasm* enclosed by a transparent, structureless membrane *(sarcolemma)*. The sarcoplasm is the cytoplasm of the muscle fiber and bathes the myofibrillae and nuclei. Mitochondria and granular elements called *sarcosomes* (exactly what they are is unknown) are present in the sarcoplasm as well as glycogen, fat and pigment. The sarcolemma, which is thin and elastic, is visible only in preparations in which the fibers are broken and twisted. The fibers show faint longitudinal striations and definite cross striations. The longitudinally striated appearance of the fibers is due to the presence of numerous bundles of delicate myofibrillae *(sarcostyles)* which extend from one end of the fiber to the other. The fluid sarcoplasm occupies the spaces between the myofibrillae.

The myofibrillae are exceedingly small, delicate threads of differentiated protoplasm which are so closely bound together in the muscle fibers that they are difficult to distinguish in ordinary preparations. The bundles of myofibrillae (sarcostyles) are also known as *muscle columns of Kölliker.* The term "sarcostyle" has been applied by some authors to the individual myofibrillae; it is more commonly used, however, to indicate the muscle columns. As they appear in cross section, the muscle columns of Kölliker are known as the *areas of Cohnheim.* These areas are separated by spaces which indicate the manner in which they are invested by sarcoplasm. Broader bands of sarcoplasm divide the areas of Cohnheim into groups.

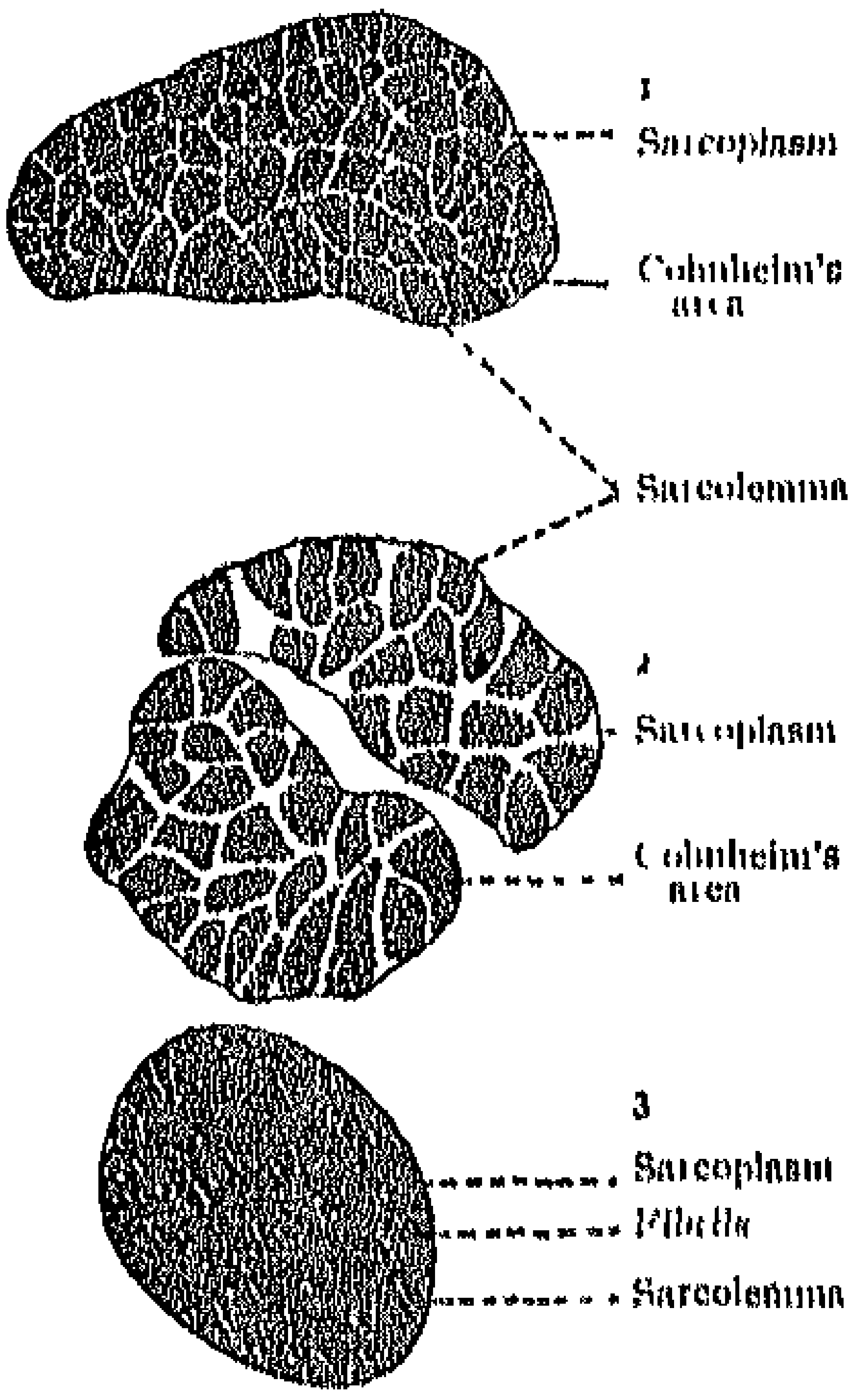


FIG. 53. Transverse section through striated muscle-fibers of a rabbit. (1 and 3) From a muscle of the lower extremity. (2) From a lingual muscle (900 X.) In 2 Cohnheim's fields are distinct; in 1 less clearly shown; in 3 the muscle fibrils are more evenly distributed. (After Böhm, Davidoff, and Huber.)

Each fiber of striated muscle has many nuclei, as many as 100 nuclei being present in the longer fibers. In mammals these nuclei are located at the periphery of the fibers and are covered by the sarcolemma. The nuclei are flattened and oval and contain a delicate network of chromatin. Each nucleus is surrounded by a small amount of granular cytoplasm.

Two kinds of striated fibers are recognized, the red and the white. Muscles in which the red fibers predominate are considerably darker than those in which the white fibers are more abundant. The color of the red fibers is due to a greater abundance of sarcoplasm, which contains a pigment *(myochrome)* to which the color is due. The lighter color of the white fibers is due to the smaller amount of sarcoplasm which they contain. The red fibers contract more slowly than the white fibers, and are more resistant to fatigue.

The nuclei in the white fibers are located at the periphery; how-

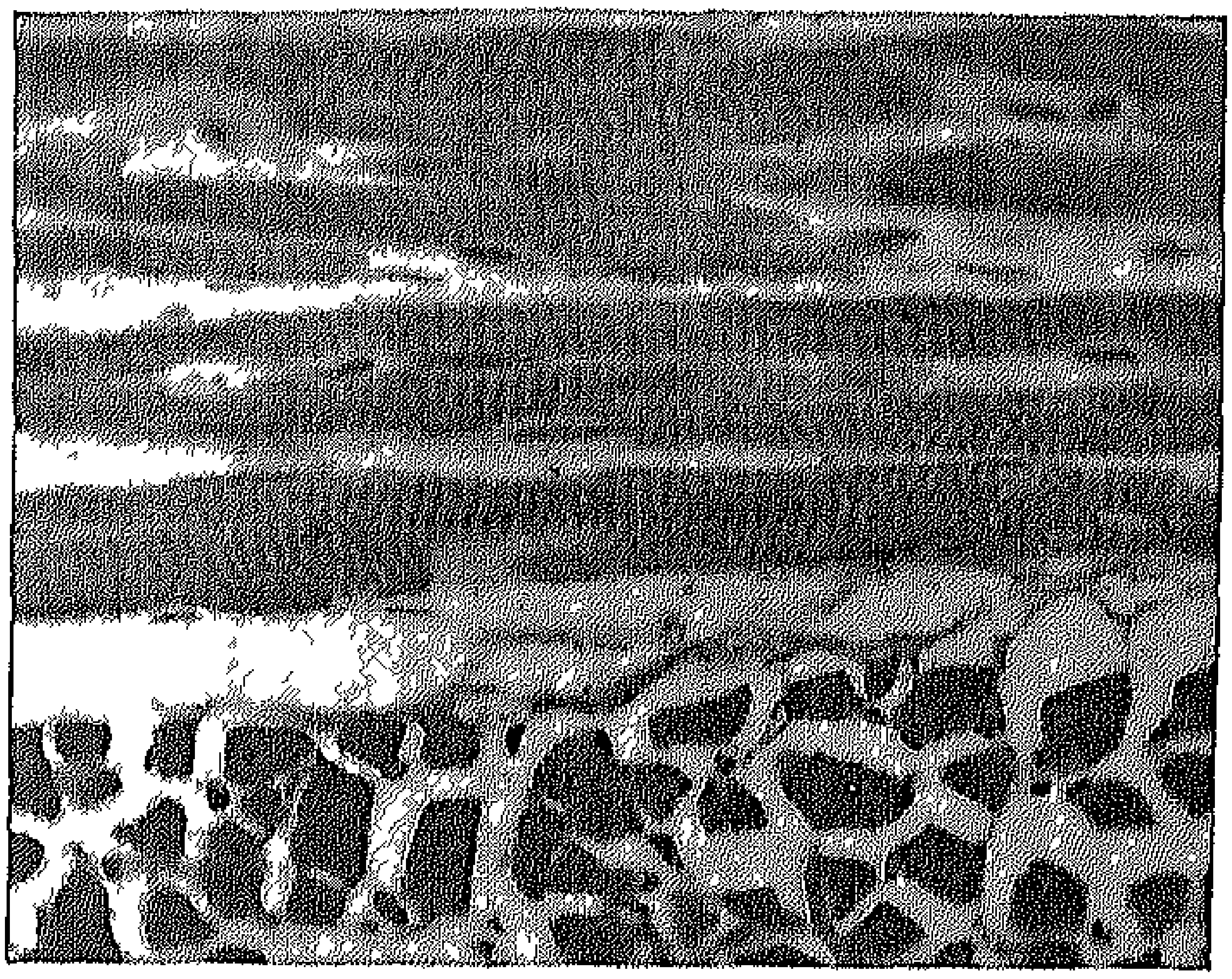


FIG. 54. Longitudinal and cross sections of striated muscle from the tongue. Hematoxylin and eosin. Photomicrograph.

ever, in the red fibers the nuclei are located more deeply within the fiber and only occasionally are found at the periphery.

Striated fibers are generally regarded as giant multinucleated cells. Some authors are inclined to consider the protoplasm which surrounds a nucleus as being continuous with that surrounding the other nuclei, thus forming a syncytium. A view which is being regarded with increasing favor, is that the nuclei represent individual cells, the myofibrillae and other structures of the fiber being extracellular. According to this view, the nuclei and the protoplasm in which they are enclosed would be comparable to connective tissue cells, the columns of Kölliker being similar in some respects to the fiber bundles of connective tissues. By this view, striated muscle is brought into a closer relationship with the connective tissues with which it takes its origin from mesenchyme.

The characteristic feature of striated muscle is its cross-banded appearance. This is due to alternate light and dark bands which cross the fibers transversely and which follow one another at regular intervals. These bands exhibit different refractive properties when viewed with polarized light. The light bands, which are singly refractive, are said to be *isotropic*, while the dark bands, which are doubly refractive, are said to be *anisotropic*. The occurrence of isotropic and anisotropic areas is not a property of the fiber as a whole, the areas being confined to the myofibrillae in which they occupy the same plane. This gives the bands the appearance of crossing the fiber.

The existence of myofibrillae in the living fiber has been questioned. Some authors hold that they are formed by the precipitation of substances in the sarcoplasm *which gel readily when acted upon by the reagents employed in preparing* muscle tissue for microscopic examination. Against this view, however, is the fact that when fresh material is teased, the myofibrillae, showing isotropic and anisotropic areas, are made to stand apart from one another at the end of the fiber.

It is difficult to distinguish all the markings which have been described for striated fibers in the muscles of the higher animals, however, they can be *identified readily in the wing muscles of certain* insects. Examination of these muscles reveals, besides the light and dark bands (designated j and q respectively), a dark line called *Krause's membrane* (designated *z*) which passes through the middle of the light band. Krause's membrane is not confined to the myofibrillae, but extends through the fiber and is attached to the sarcolemma. A light area which appears in the middle of the dark band, is known as Hensen's disc. A fine, dark line passing through the middle of Hensen's disc is known as Hensen's line (designated m).

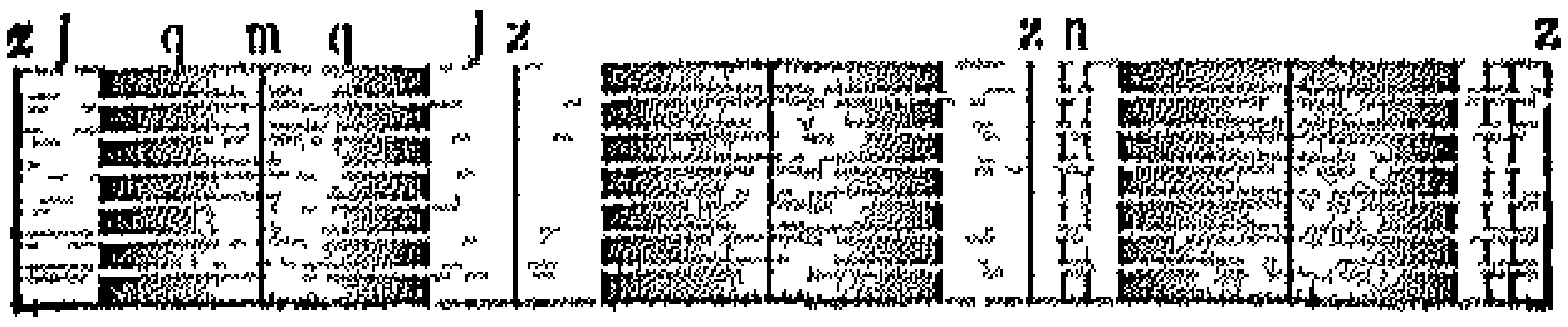


FIG. 55. Diagram of muscle striations (after Heidenhain). The fibrils consist of alternating dark bands (q) and light bands (j). j is traversed by the ground membrane (*z*) and q by the median membrane (m). In the right of the three muscle segments shown in the figure, the bands (n) have been drawn. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

The portion of the fiber between two Krause's membranes contains an entire anisotropic band with one-half of an isotropic band on either side. This constitutes a *sarcomere* or *muscle segment of Bowman*. Each such segment is regarded as a unit of contraction of the fiber.

Some investigators believe that the myofibrillae are homogeneous structures and that the cross striations are produced by the presence of granules (of different chemical composition) in the sarcoplasm. This claim is not as yet generally accepted.

CONTRACTION OF STRIATED MUSCLE. When a striated muscle fiber contracts, it may reduce its length one-tenth with an increase in its diameter (volume remains unchanged). During this contraction the cross striations become narrower and are closer together, the longitudinal striations are more pronounced, and the myofibrillae become thicker.

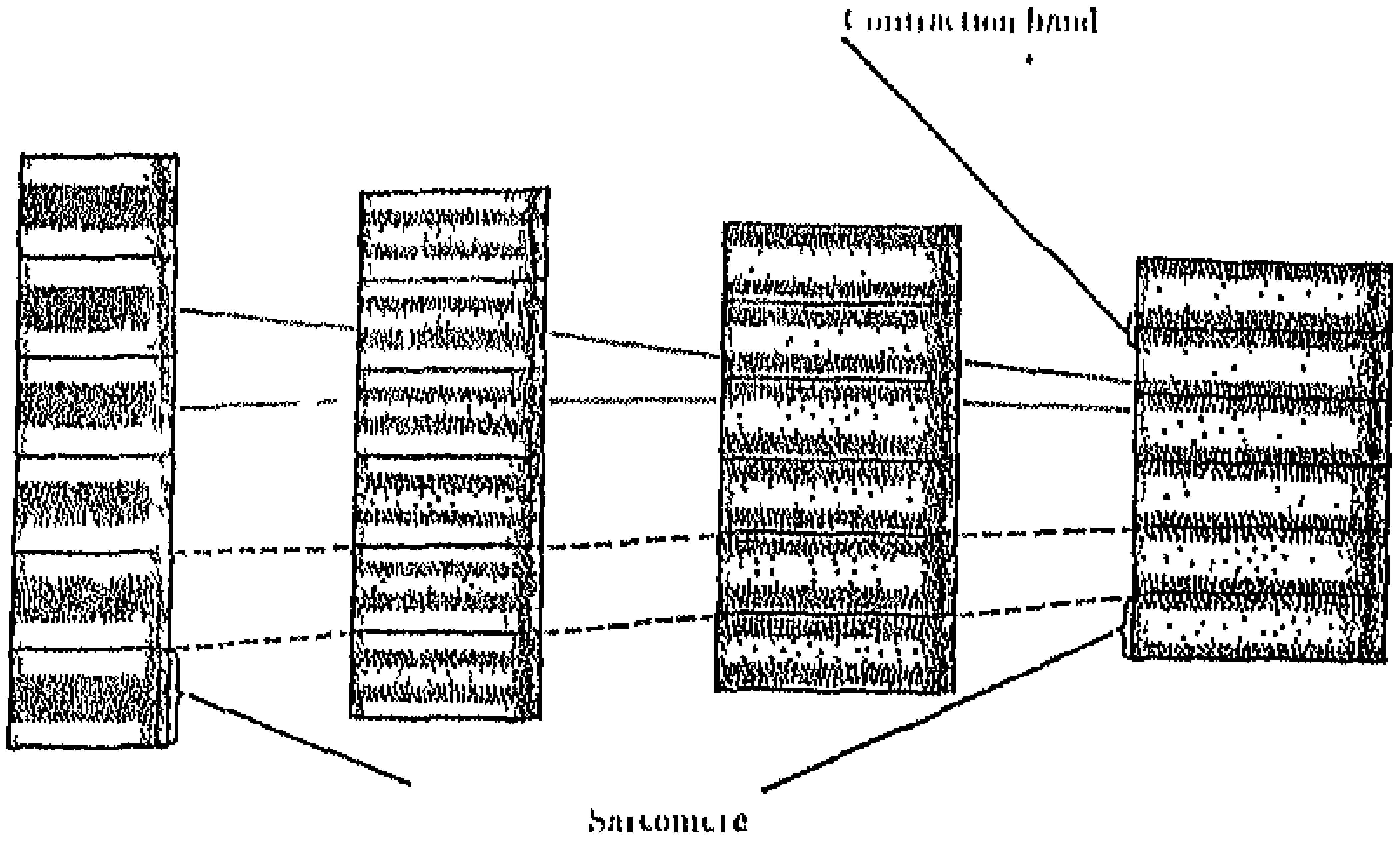


FIG. 56 Diagrams to illustrate four successive stages in the contraction of a striated muscle fibril.

In the relaxed muscle the q and j bands are about equal in width. When contraction starts a light area appears (H band) which bisects q. Further contraction results in the bisected q segments moving apart, thereby causing a widening of the H band. As this separation of the q segments continues it results in the q segments of this particular sarcomere approaching the neighboring q segment of adjacent sarcomeres. With contraction complete the q segments have reached the end of the sarcomere which is represented by the z lines. The adjacent q segments fuse to form a *contraction band*. The z line, at this point, is completely hidden by the q segments. With relaxation there is a return to the original arrangement. Chemical changes take place during the contraction of muscle fibers. The breakdown of phosphocreatine into creatine and phosphoric acid produces the actual contraction. Carbohydrate (glycogen) breaks down to lactic acid. Oxygen is used and carbon dioxide is formed. This reaction produces energy which is necessary for the resynthesis of phosphocreatine.

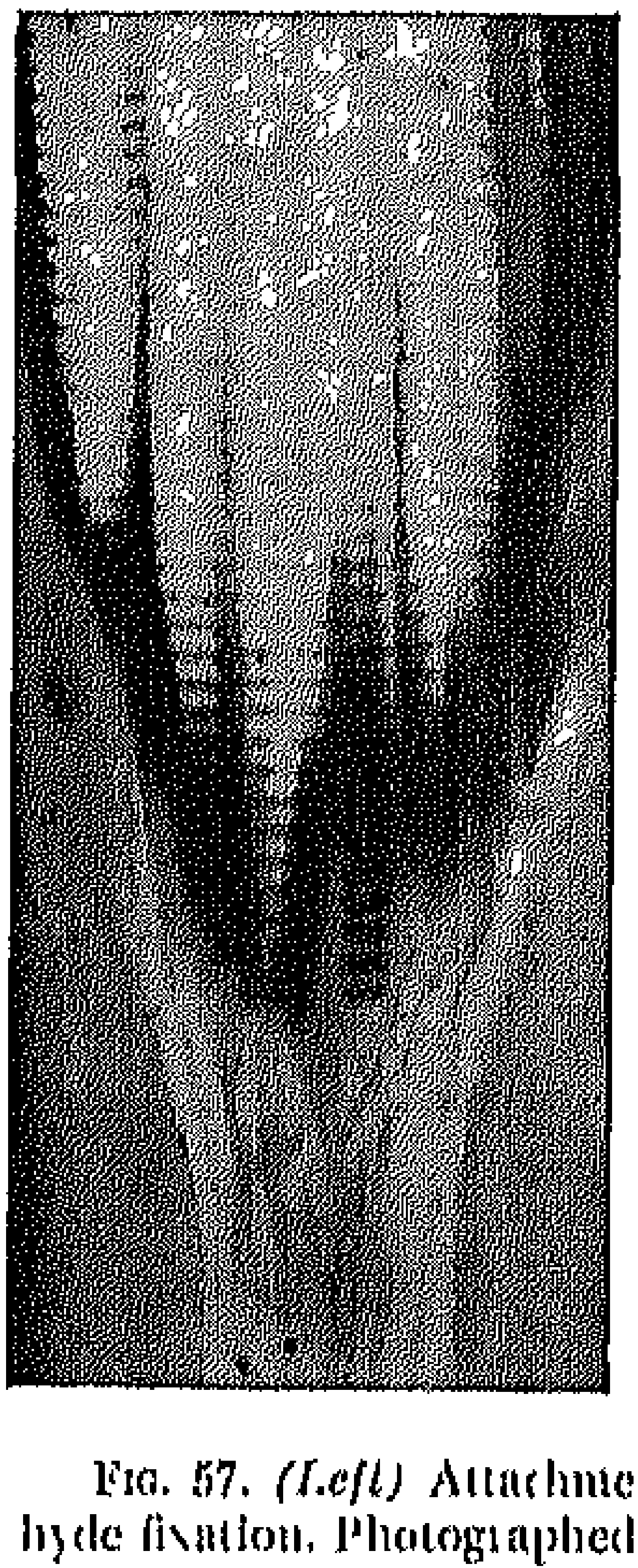
REGENERATION OF STRIATED MUSCLE. In the higher vertebrates there is very little regeneration of functional striated muscle fibers. Regeneration of partially destroyed or injured fibers has been described but it requires the presence of the intact sarcolemma sheath, the nuclei and an outer layer of sarcoplasm. From the damaged end of such a fiber, a branched pseudopodium is sent out, carrying nuclei with it. Myofibrillae and cross striations are not present in this newly forming sarcoplasm but develop later. Severe damage to striated muscle is repaired by scar tissue.

CARDIAC MUSCLE

Cardiac muscle is a specialized form of muscle, capable of contracting automatically and rhythmically. It is found only in the heart and the roots of the large vessels springing from the heart. Its fibers are arranged in layers in which they are more or less parallel. These layers, which begin at the atrioventricular junction, form loops about the ventricles so that fibers in one layer cross those of another layer in different directions. Therefore, in sections of heart muscle (myocardium), fibers will appear which have been cut longitudinally, diagonally and transversely.

Cardiac muscle differs from both smooth and skeletal muscle in having its fibers branch and the presence of intercalated discs. The branches anastomose with one another or with adjacent fibers and form a syncytium. In the branches, the myofibrillae cross from one fiber to another. However, there are no anastomoses of the myofibrillae; those from one fiber continue with the myofibrillae of the fiber which they have joined. The intercalated discs are discussed later.

Cross striations are present in cardiac muscle. They are similar



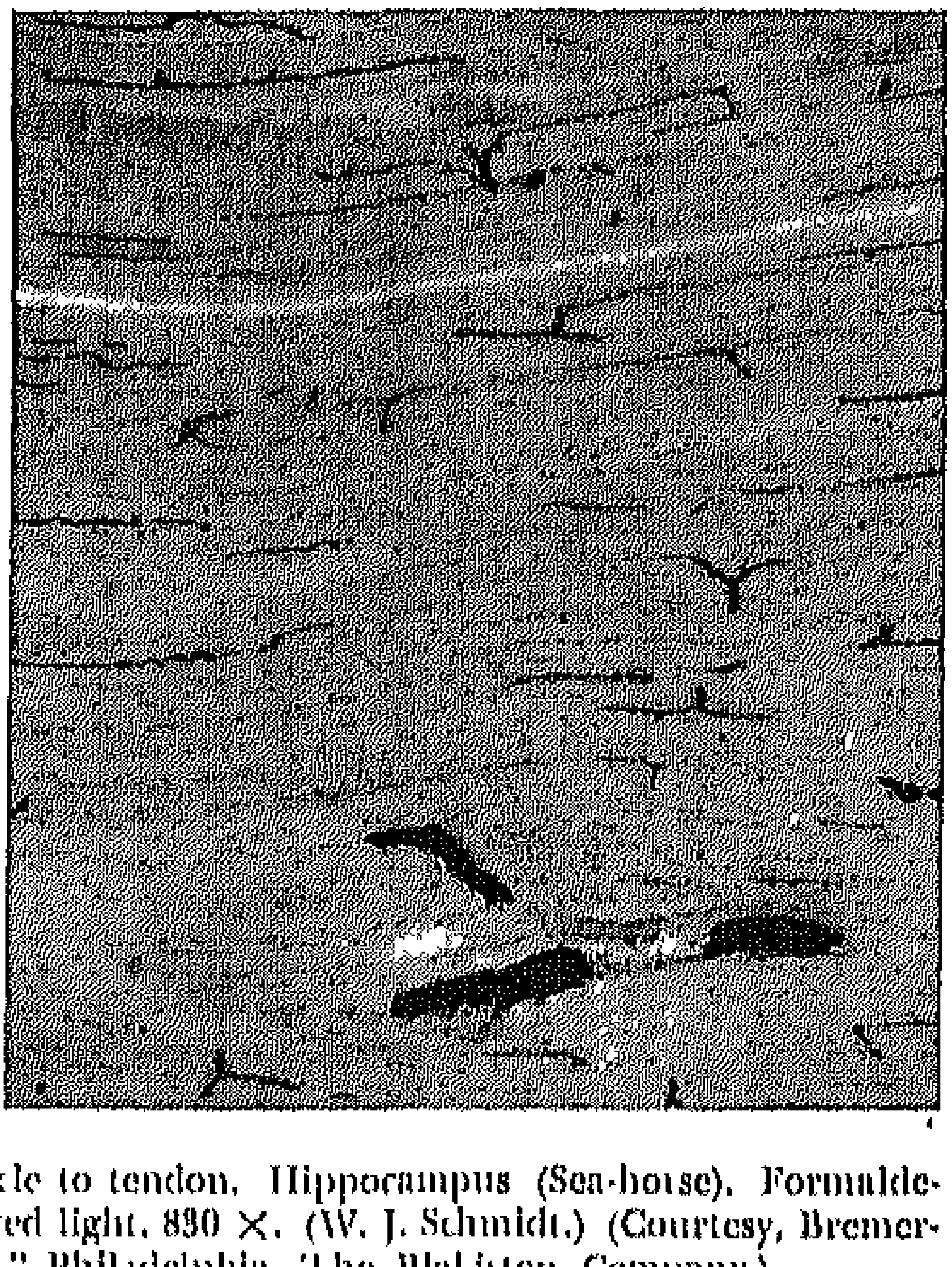


Fig. 57. *(Left)* Attachment of muscle to tendon. Hippocampus (Sea-horse). Formaldehyde fixation. Photographed in polarized light. 890 ×. (W. J. Schmidt.) (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

Fig. 58. *(Right)* Striated muscle, injected, showing the relation of the capillaries to the muscle fibers. Photomicrograph.

to those found in skeletal muscle but are less distinct. There are many nuclei in each fiber and the nuclei are large, oval in outline, and are frequently elongated. The nuclei are located in the center of the fiber as in smooth muscle. Their structure is similar to that of striated muscle nuclei. The cytoplasm of the cell is accumulated at either end of the nucleus and merges with the *surrounding sarcoplasm.* The cytoplasm contains granules, mitochondria and droplets of fat. The myofibrillae are arranged in rows, which extend from the periphery to the center of the fiber; this arrangement gives them the appearance of the spokes of a wheel when a crosscut section is observed. Sarcoplasm fills the spaces between the myofibrillae. The fibers are enveloped by a very thin membrane not unlike the sarcolemma of striated muscle. Sarcosomes are abundant in cardiac muscle.

The most characteristic feature of cardiac muscle is a number of dark bands, the *intercalated discs,* which cross the fibers at irregular intervals. They may extend partially or completely across the fiber either as a straight line or in a series of steps.

Various theories have been presented to account for the intercalated discs. They were first thought to represent the end boundaries of the muscle cells, but with the absence, in many instances, of a nucleus between two discs, and in other cases, with two or more discs crossing a single nucleus, this view has been abandoned. With the discovery that similar discs may appear in other than heart muscle, the idea that they are related in some way to the contraction of the fiber is receiving increased support.

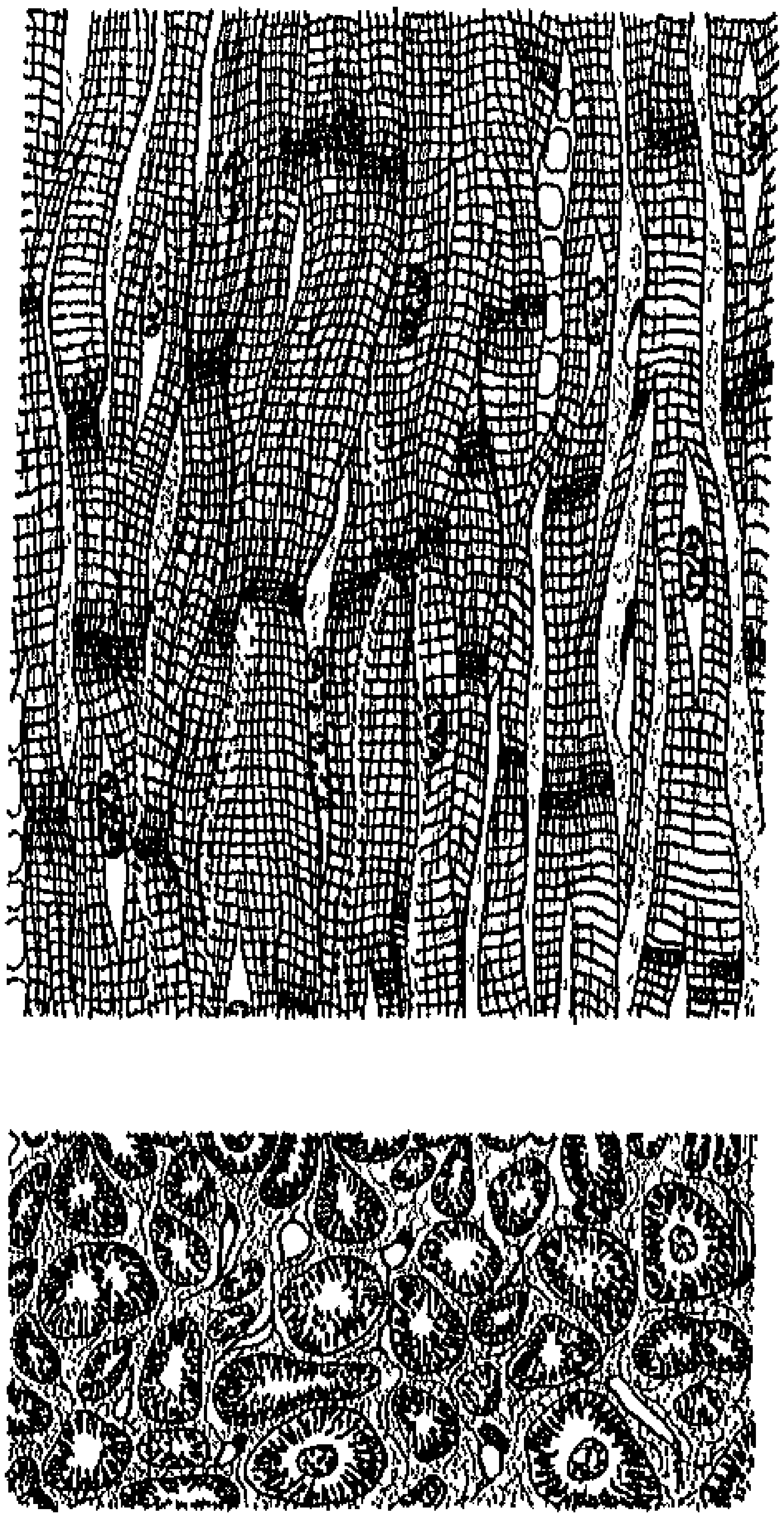


FIG. 59 Cross and longitudinal section of cardiac muscle. The longitudinal section shows the branching and anastomosing of the fibers Note the centrally located nuclei.

Intercalated discs are absent from or are only poorly developed in young hearts. They apparently increase as age advances. That they

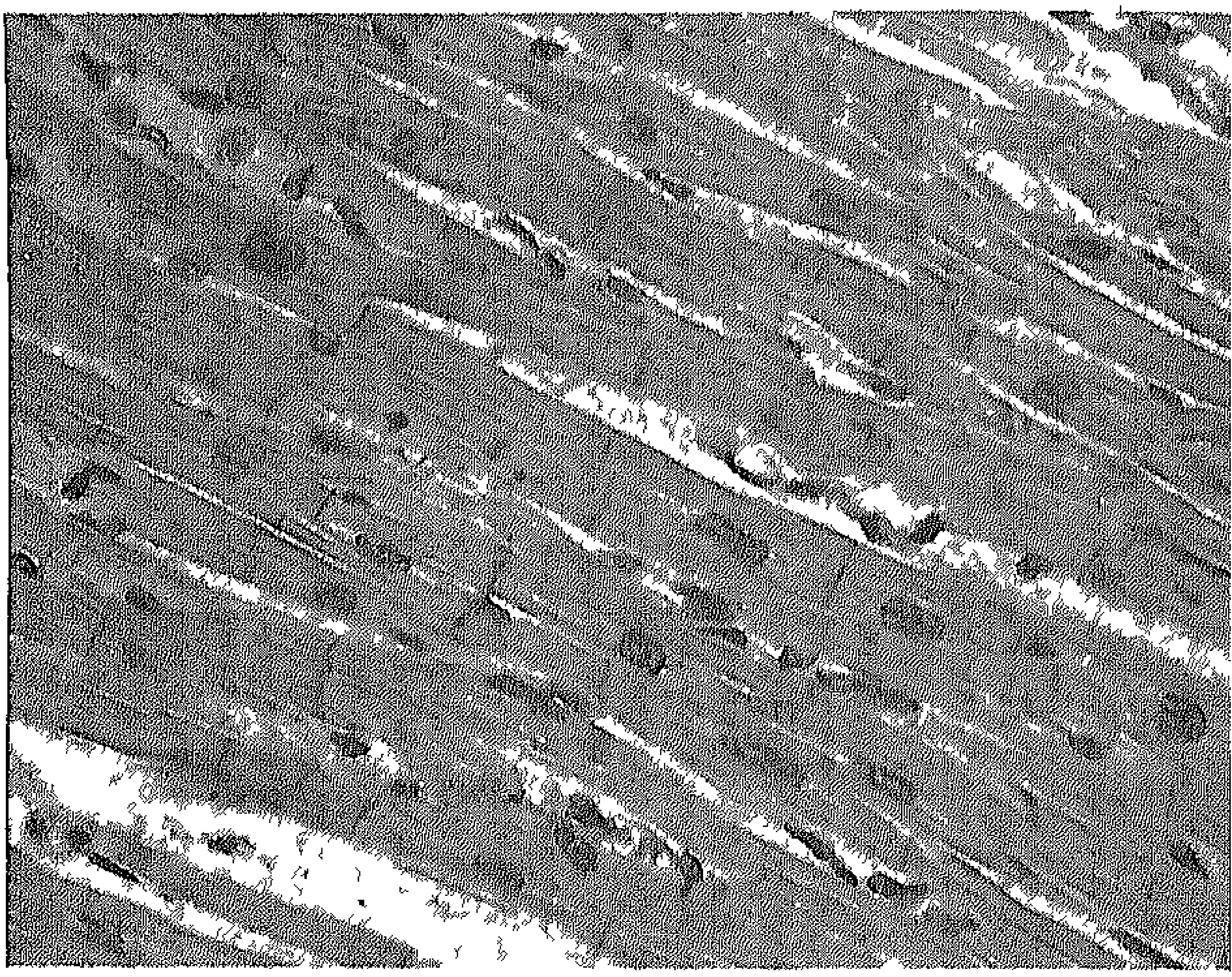


FIG. 60. Longitudinal section of human cardiac muscle. Observe the centrally located nuclei and the dark transverse lines which are the intercalated discs. Photomicrograph.

constitute an area of weakness in the fiber is indicated by the fact that when heart muscle is fragmented, the lines of fragmentation occur in the areas of the intercalated discs.

Certain fibers of the heart muscle are specialized as neuroepithelial elements to transmit the impulse for contraction. These atypical fibers are known as *Purkinje fibers*. These fibers differ from ordinary cardiac muscle in their greater size and the possession of considerably more sarcoplasm. The myofibrillae are reduced in number and are located about the peripheral portion of the fiber. The bundle is enclosed by a sheath of connective tissue, by which it is separated from the myocardium.

REGENERATION OF CARDIAC MUSCLE. The power which cardiac muscle has for regeneration is practically nil. Any marked damage of cardiac muscle is replaced by scar tissue. In areas where the damage is not severe evidences may be seen of where cells have made abortive efforts to regenerate.

SUMMARY

DEFINITION: The muscles are the contractile tissues of the body.

COMPOSITION: 1. Fibers (muscle cells, fibrillae, fluid proto-

plasm or sarcoplasm, and some type of cell membrane)
2. Connective tissue (sheath and septa)

BASIS OF CLASSIFICATION: 1. Structure
- a. Striated
- b. Nonstriated

2. Function
- a. Voluntary
- b. Involuntary

TYPES OF MUSCLE: 1. Smooth (nonstriated and involuntary)
2. Striated (striated and voluntary)
3. Cardiac (striated and involuntary)

DIFFERENTIAL CHARACTERISTICS OF MUSCLE

Type	*Fiber*			*Nucleus*		
	Shape	*Cross Striations*	*Other Characteristics*	*Location*	*Shape*	*Size and Number*
Smooth (involuntary)	Fusiform	None	Cell membrane	Center of fiber	Oval	Relatively large — almost fills entire diameter of fiber One nucleus to a fiber
Striated (voluntary)	Cylindrical	Present	Sarcolemma Fibers do not branch	Periphery of fiber	Oval	Medium size Many to a fiber
Cardiac (involuntary)	Cylindrical	Present	Cell membrane Fibers branch Intercalated discs Shows property of automatism	Center of fiber	Plump Oval	Medium size Many to a fiber

9

The Nervous System

All protoplasm exhibits the properties of irritability and conductivity, but only in the tissue of the nervous system do these properties reach their highest degree of development and specialization. To these two fundamental properties may be added another, correlation, which is exhibited only by the nervous system.

The function of the nervous system is to receive *stimuli* from the surface or from the various organs of the body, transmit them to the brain or cord, and effect the necessary motor response. In this way the body is able to adjust to an everchanging environment.

The nervous system consists of: the *brain* and *spinal cord* (the central nervous system), the *peripheral nerves* (made up of the axons of the nerve cells), the *autonomic* system (made up of the sympathetic and parasympathetic systems of nerves and their ganglia), and the specialized receptor organs for sensory stimulations, the *sensory end organs*. Associated with these specialized cells of the nervous tissue and their fibers is a specialized type of connective tissue *(neuroglia)* which serves to support and bind together the component elements.

The functional and physiological unit of the nervous tissue is the nerve cell or *neuron*. These cells are found only in the substance of the brain or cord, where they are localized in certain definite areas (nuclei of the brain; gray matter of the cord), and outside of the central nervous system in organized structures known as *ganglia*. Each nerve cell consists of a cell body and its processes, the axon and dendrites. These processes are capable of receiving and transmitting the nerve impulses. According to the number of processes which they possess, neurons are known as: *unipolar*, *bipolar*, and *multipolar neurons*. Unipolar cells are those which have only a single process. Cells of this type occur in the ganglia of the cranial and spinal nerves. It has been questioned whether or not these cells may properly be regarded as unipolar, since they are bipolar in the embryo. In the adult, the two processes of the embryonic cell unite to form a single process which divides a short distance from the cell body into a peripheral and central branch. The peripheral branch transmits impulses toward the cell body; the central branch, away from the cell body. The peripheral branch is usually referred to as an axon, however, since it possesses the characteristics of an axon. Some people consider this branch as a dendrite, but on the basis of the morphology of this fiber and the fact that axons can transmit impulses in either direction throughout their length, it seems best to consider this as an axon, not a dendrite.

Bipolar cells are more or less spindle-shaped with two processes, one of which is a dendrite and the other an axon, extending from either end, or pole, of the cell. Cells of this type are found in the retina of the eye, the vestibular and spinal ganglia of the ear, and numerous places in the central nervous system.

Multipolar cells constitute the greater number of the cells of the nervous system. Each multipolar cell, in addition to its axon, possesses two or more dendrites. The manner in which these processes arise from the cell body gives it a stellate appearance.

The transmission of a nervous impulse (in vertebrates) from the point of stimulation to the effector organ, requires at least two neurons. The impulse passes from the axon of the first neuron to the dendrite or cell body of the second neuron. For this to take place these two processes must be in contact with one another, and the point of contact is known as a *synapse*. While an impulse may be transmitted in either direction within any single neuron, the synapse will allow the impulse to pass in only one direction, from axon to dendrite. This arrangement assures the "one-way" transmission to the central nervous system and out again to the effector organ. This "tandem" arrangement of the two neurons for the transmission of an impulse is known as a *reflex arc*. While a two neuron reflex represents, theoretically, the simplest reflex arc, with few exceptions (knee jerk) it is not found in man. A more common type of reflex arc in the human involves at least three neurons. This third neuron, which is located between the sensory and motor neurons, is called an *association neuron*, providing it starts and ends on one side of the cord. However, if this third neuron crosses from one side of the cord to the other it is known as a *commissural neuron*. These neurons may also ascend or descend to other segments of the cord, thereby integrating various regions, and they always lie within the substance of the gray matter of the spinal cord.

Gross examination of a cross section of the cord shows two distinct areas. In the center of the cord is a gray or pinkish gray column of tissue, shaped roughly like the letter H. This is made up chiefly of nerve cells, portions of dendrites and axons, and unmyelinated fibers. This gray column is entirely surrounded by a layer of whitish colored tissue. Myelinated nerve fiber "tracts" are found in the white substance which forms this outer layer. Supporting the elements in both areas is the connective tissue called neuroglia. The size and shape of the

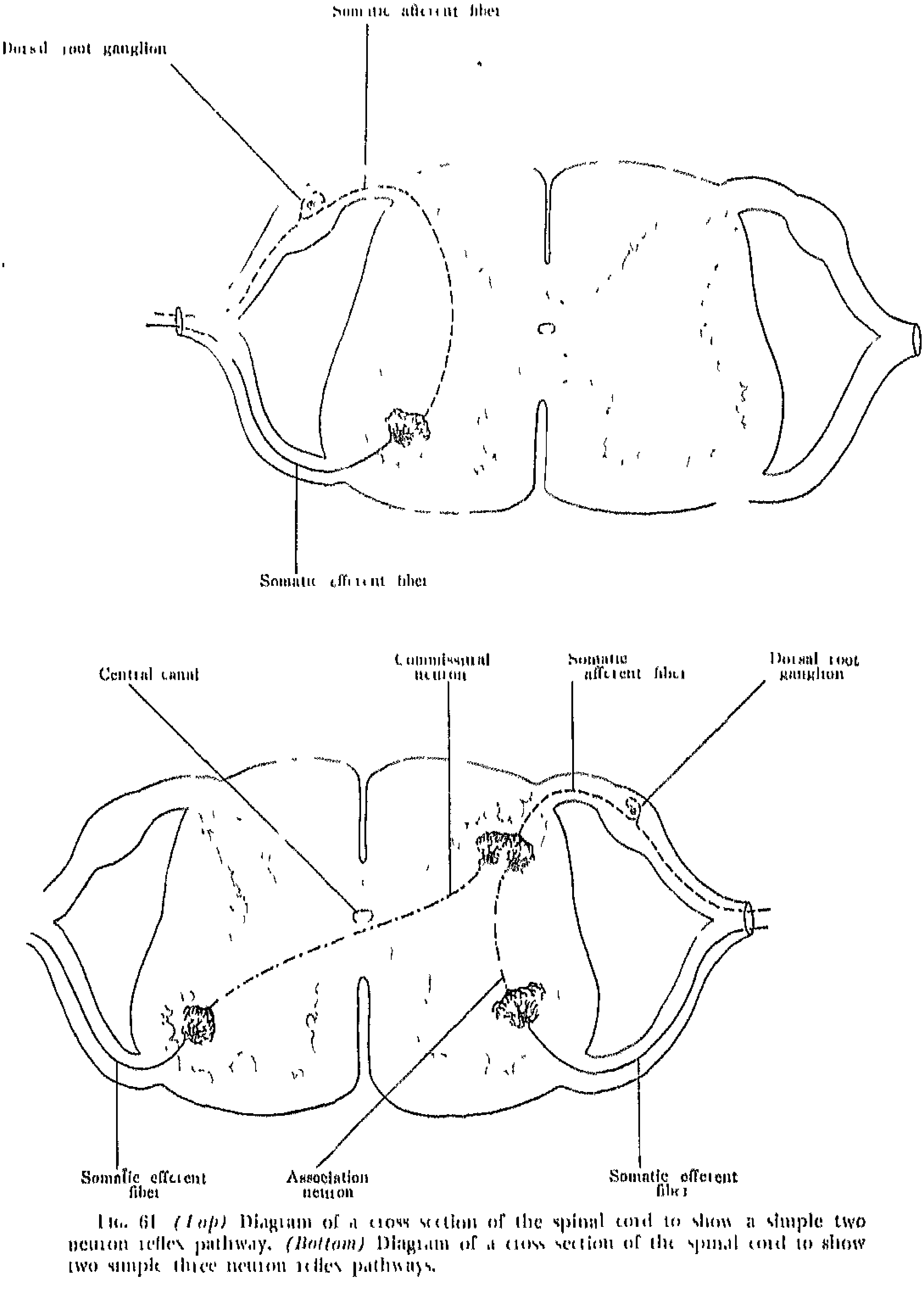


Fig. 61 *(Top)* Diagram of a cross section of the spinal cord to show a simple two neuron reflex pathway. *(Bottom)* Diagram of a cross section of the spinal cord to show two simple three neuron reflex pathways.

column of gray matter and the amount of the white substance varies slightly throughout the length of the cord.

From the antero- and postero-lateral surfaces of the spinal cord, throughout its length, are given off thirty-one pairs of spinal nerves. They leave the spinal canal by way of the intervertebral foramina. Each spinal nerve has a ventral or motor root and a dorsal or sensory root. The cell body of the dorsal root neuron is located in the dorsal root ganglion, which lies just outside the spinal cord. The cell bodies of the ventral root neurons are found within the gray substance of the cord.

It is possible to classify the nerve fibers according to function as: visceral afferent, visceral efferent, somatic afferent, and somatic efferent, depending on whether these fibers serve the viscera and blood vessels or all other structures of the body exclusive of these two.

While the visceral efferent fibers are found as elements of the spinal nerves, in reality they are a part of the so-called autonomic division of the nervous system (an efferent system). In order to reach their destination, visceral efferent impulses must travel over two visceral efferent neurons. The neuron of the first order has its cell body in the cerebrospinal axis and its preganglionic myelinated fiber goes by way of the white rami to terminate in a sympathetic ganglia.

The cell body of the second order neuron lies in the sympathetic ganglion and its postganglionic, unmyelinated fiber ends in the structure it innervates. Occasional postganglionic fibers have thin myelin sheaths. These postganglionic fibers may go either directly to a viscera of the abdominal region or they may enter the peripheral portion of spinal nerves by way of the gray rami and be distributed to smooth muscle, blood vessels, sweat glands, the arrector pili muscles of hairs, etc. Besides the unmyelinated visceral efferent fibers, the peripheral portion of spinal nerves also carry unmyelinated somatic afferent fibers (pain fibers).

Visceral afferent fibers have their cell bodies in the spinal ganglia. However, these visceral afferent fibers also run by way of the white rami of the thoracic and upper lumbar nerves. The white rami also contain preganglionic visceral efferent fibers.

The somatic efferent fibers send motor impulses to skeletal muscle. The cell bodies of these fibers (axons) are located in the spinal cord. Somatic afferent fibers may be classified, according to the source of their stimuli, as *proprioceptive fibers* or *exteroceptive fibers.* The proprioceptive fibers receive their stimuli from end organs in muscles, joints, and tendons. The exteroceptive fibers receive their stimuli from the outside environment by way of the skin, eye and ear. Included also in this group are those fibers which carry impulses produced by "pressure-touch" stimuli which are located deep to the surface of the skin.

AUTONOMIC NERVOUS SYSTEM

The autonomic nervous system is an efferent (motor) system composed of nerves, ganglia and plexuses, supplying the viscera and the vascular system. It conveys impulses which, for the most part, are not reflected in consciousness, but direct and control the movements of organs not subject to the will (although psychic influences are possible), hence, it may be regarded as the *involuntary* part of the nervous system. It is important to realize that this is purely a functional division, not an anatomical division of the nervous system.

In the autonomic system, two neurons are required in order for an impulse to reach the effector organ from the central nervous system. The cell body of the first neuron lies in the gray substance of the brain or cord; the cell body of the second neuron lies in either the sympathetic ganglion or within the tissue of the effector organ. The axon of the first neuron is known as a *preganglionic fiber,* while that of the second neuron is called a *postganglionic fiber.* The preganglionic myelinated fibers enter the peripheral nerves by way of the white rami (the white rami also contain visceral afferent fibers). There are also unmyelinated postganglionic fibers which enter the peripheral nerves by way of the gray rami. Autonomic nerve fibers are found in five of the cranial nerves (third, seventh, ninth, tenth, and eleventh) and in all of the spinal nerves.

It is customary to divide the autonomic system into two separate divisions: the *sympathetic* and the *parasympathetic.* The sympathetic division is composed of the visceral efferent fibers of the thoracolumbar segments of the cord; whereas the parasympathetic division is composed of craniosacral segments. Until recently the effects of the sympathetic and parasympathetic systems have been thought to be antagonistic to one another, (in general, that the sympathetic fibers caused constriction of smooth muscle and the parasympathetic caused relaxation), but the number of exceptions to these reactions in specific instances has opened this "antagonistic" theory to further investigations and analysis.

An excellent discussion on this subject is given by Langworthy and the following discussion is based on his paper.

The functions of these two divisions are not antagonistic, but rather they supplement each other. The sympathetic system innervates the smooth muscle of the vascular system, while the parasympathetic fibers with certain exceptions (heart muscle and genital duct system), are distributed to all other smooth muscle of the body (viscera). This delegation of specific areas of control is based on experimental evidence.

Since the sympathetic fibers are distributed to the vascular system, they extend to all parts of the body. (Experimental evidence has not shown that parasympathetic fibers are distributed to the peripheral vascular system or that vessels are supplied by fibers that will produce dilatation, however, dilatation can be produced by nervous activity.) The organization of the sympathetic system is such that it exhibits a "total" response in its reaction to stimuli. The parasympathetic system, on the other hand, shows a more specific type of response since it

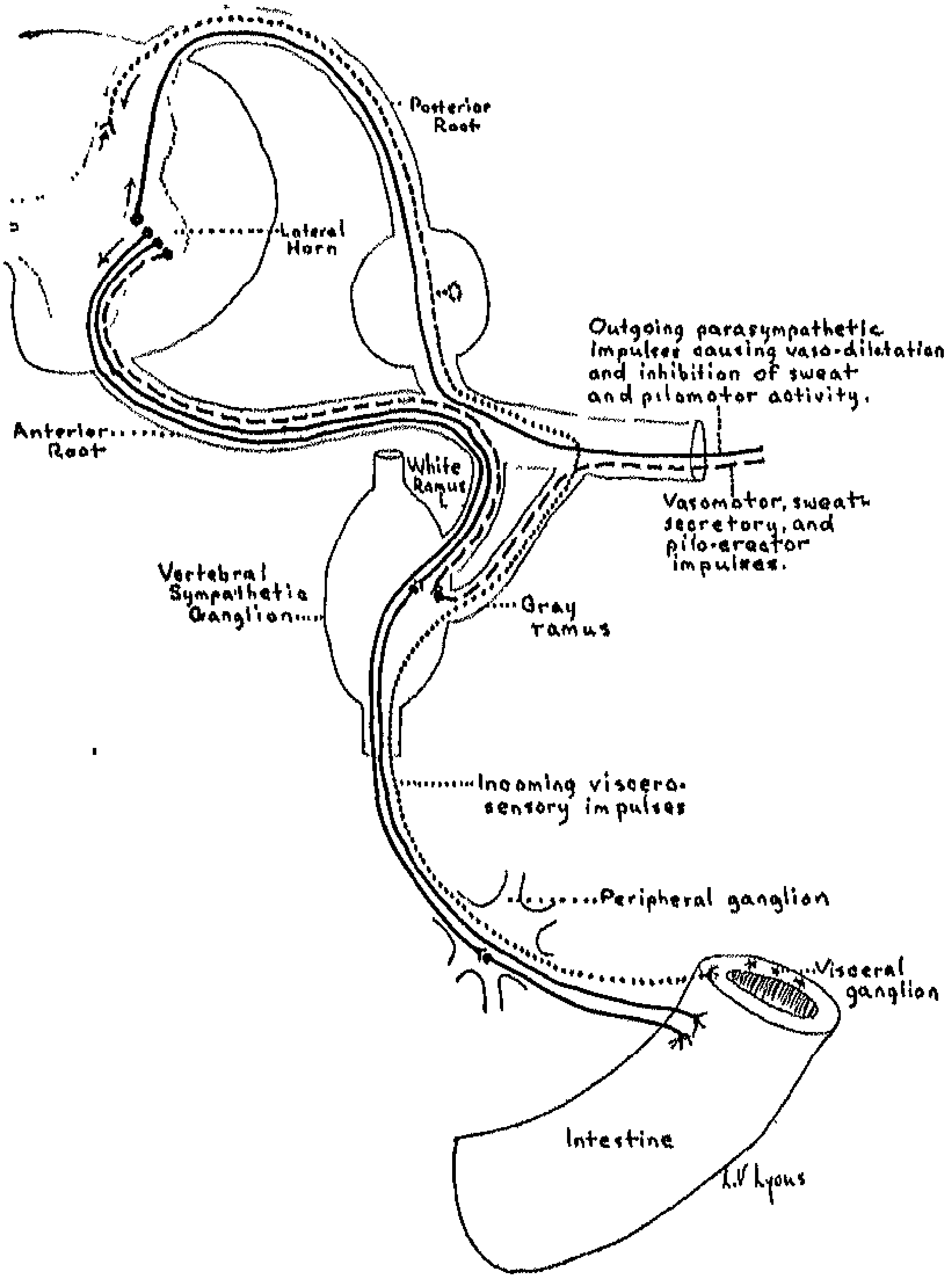
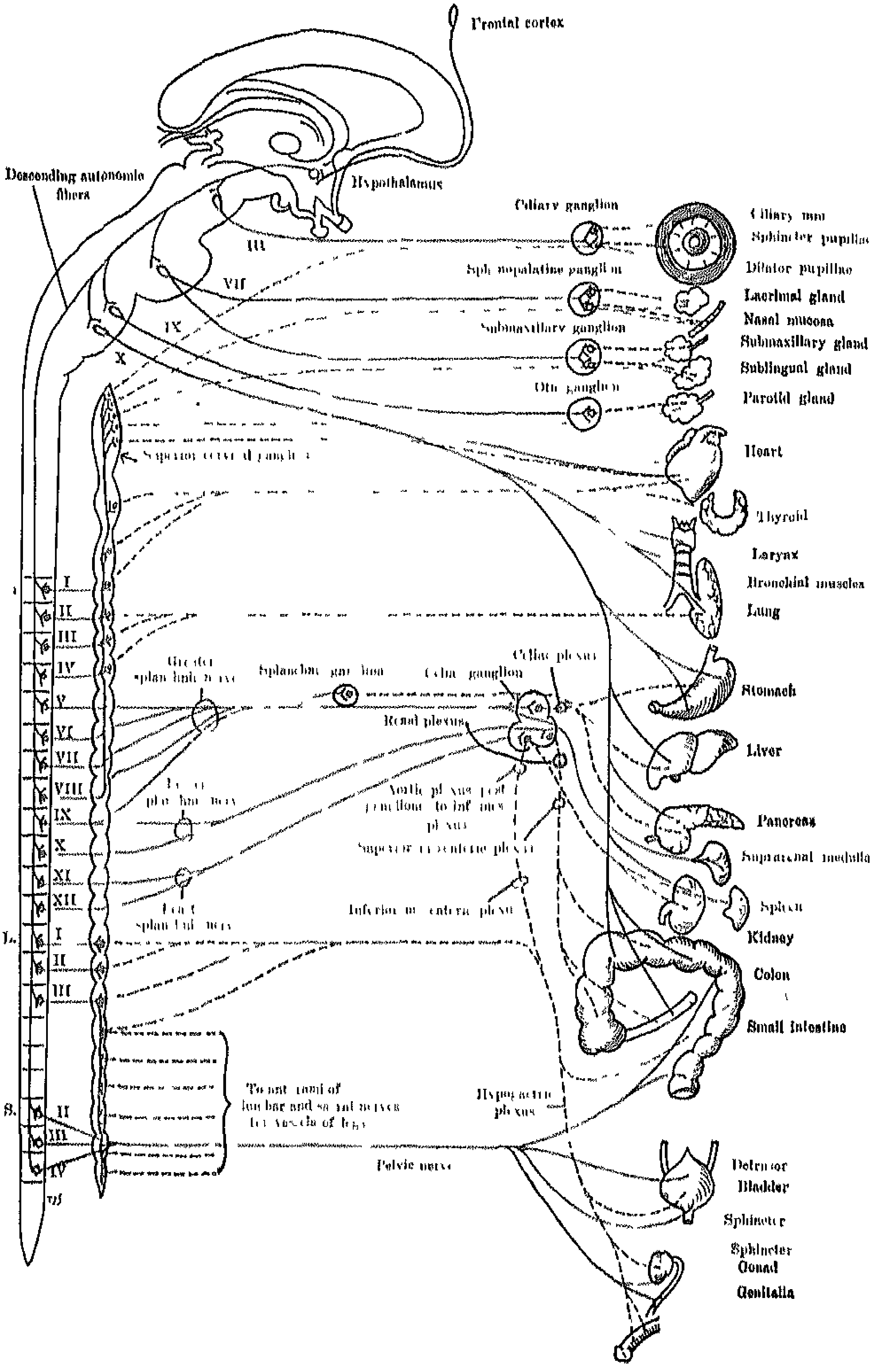

Posterior Root
Lateral Horn
Outgoing parasympathetic impulses causing vaso-dilatation and inhibition of sweat and pilomotor activity.
Anterior Root
White Ramus
Vasomotor, sweat-secretory, and pilo-erector impulses.
Vertebral Sympathetic Ganglion
Gray ramus
Incoming viscero-sensory impulses
Peripheral ganglion
Visceral ganglion
Intestine
L.V. Lyons

FIG. 62. *Diagram of spinal sympathetic and spinal parasympathetic pathways. Modified from L. R. Müller.* (Courtesy, Brock: "Basis of Clinical Neurology," Baltimore, The Williams & Wilkins Co.)


Frontal cortex
Descending autonomic fibers
Hypothalamus
III
VII
IX
X
Ciliary ganglion
Ciliary mm
Sphincter pupillae
Dilator pupillae
Sphenopalatine ganglion
Lacrimal gland
Nasal mucosa
Submaxillary ganglion
Submaxillary gland
Sublingual gland
Otic ganglion
Parotid gland
Superior cervical ganglion
Heart
Thyroid
Larynx
Bronchial muscles
Lung
I
II
III
IV
V
VI
VII
VIII
IX
X
XI
XII
L.
I
II
III
S.
II
III
IV
Greater splanchnic nerve
Splanchnic ganglion
Celiac ganglion
Celiac plexus
Renal plexus
Stomach
Liver
Lesser splanchnic nerve
Aortic plexus post ganglionic to inf mes plexus
Superior mesenteric plexus
Pancreas
Suprarenal medulla
Least splanchnic nerve
Inferior mesenteric plexus
Spleen
Kidney
Colon
Small intestine
To gray rami of lumbar and sacral nerves for vessels of legs
Hypogastric plexus
Pelvic nerve
Detrusor
Bladder
Sphincter
Sphincter
Gonad
Genitalia

innervates specific organs, and only a part of this system may react at a time. This may also imply the presence of a more differentiated type of end organ for the parasympathetic system.

The idea of antagonistic action by these two systems gains support from the fact that some organs receive innervation from both systems. Where this occurs it is likely that the sympathetic fibers supply blood vessels and any reaction that may result from their stimulation is due to change in amount of blood to the organ. The bladder is such an organ. In the bladder it was thought that the parasympathetic fibers produced relaxation of the internal vesical sphincter muscle and contraction of the smooth muscle of the bladder wall, causing it to empty itself. Likewise, it was thought that the sympathetics caused the bladder muscle to relax and the internal sphincter muscle to constrict, thereby closing the orifice and allowing the organ to fill again. However, experimental studies have shown that the sympathetic fibers to the bladder can be cut without any important effect on the function of the organ. Damage to the parasympathetic fibers, however, effected complete paralysis of the muscle, and while, in time, some of the function returned, the function of the organ was seriously impaired. Other examples of misinterpretation of the antagonistic functions of these two systems are cited by Langworthy.

SYMPATHETIC DIVISION. The sympathetic trunks consist of two ganglionated trunks which start at the level of the second cervical vertebra and terminate at the level of the coccyx. They are located just anterior and lateral to the bodies of the vertebrae.

Each sympathetic trunk is made up of a series of twenty-one or twenty-two ganglia (three cervical, ten or eleven thoracic, four lumbar and four sacral), which are connected by a bundle of nerve fibers made up of ascending and descending nerve fibers. Fine bundles of nerve fibers *(connecting rami)* connect each spinal nerve with the sympathetic trunk of its respective side.

The sympathetic trunk sends unmyelinated postganglionic fibers by way of the gray rami to each spinal nerve. White rami, however, carry myelinated preganglionic fibers from a limited number of spinal nerves (all of the thoracic, and the second to fourth lumbar nerves to corresponding sympathetic ganglia chain or collateral). White rami also contain fibers bearing sensory impulses from the viscera. The fibers from the sympathetic system innervate blood vessels. This system is largely responsible for the "emergency" response of the body. It

FIG. 63. Diagram of the autonomic system. Connections to the cutaneous vessels and sweat glands are not shown here (modified from Mettler). *Solid lines* indicate preganglionic fibers; *broken lines*, postganglionic; *green*, parasympathetic; *red*, orthosympathetic; *blue*, central conduction systems (a series of short relays under the influence of the hypothalamus and cerebral cortex). (Courtesy, Merritt-Mettler-Putnam: "Fundamentals of Clinical Neurology," Philadelphia, The Blakiston Company.)

responds to the reactions of fear, rage, pain, and muscular exercise. This system is probably the highest integrative mechanism in the hypothalamus.

PARASYMPATHETIC DIVISION. The parasympathetic division is made up of fibers derived from the third, seventh, ninth, tenth, and eleventh cranial nerves and fibers from the second, third and fourth sacral spinal nerves. The parasympathetic fibers that are components of the cranial nerves send fibers to innervate the constrictor muscle of the eye, the salivary glands, lungs, heart and the upper part of the alimentary tract. From the sacral segment, fibers are distributed to the lower part of the alimentary tract, the urinary bladder and erectile organs. The fibers of the parasympathetic system produce contraction of smooth muscle and slow the heart.

10

Nervous Tissues

The nervous tissues are composed of *nerve cells, nerve fibers,* and a form of supporting tissue called *neuroglia,* which is peculiar to the nervous system. Specialized structures known as *end sense organs* are associated with nerve endings in various parts of the body and receive the sensory stimuli.

NERVE CELLS OR NEURONS

The nerve cells and their processes (neurons) are the functional elements of the nervous tissues. They are located in the gray matter of the brain and spinal cord, in the ganglia of the cranial and spinal nerves, and in the ganglia of the sympathetic system. They vary considerably in shape and size. The form of a nerve cell depends to some extent on its location, and also on the function which its impulse serves. While the majority are stellate in form, some are round or oval, some spindle-shaped, and others are triangular in outline. The smallest cells of the nervous system have a diameter of 4–5 microns, while the largest are visible without the aid of a lens, their diameter being about 150 microns. The largest cells in the gray matter of the ventral horn of the spinal cord are about 130 microns in diameter.

Nerve cells possess a nucleus around which is the cytoplasm, the same as other cells of the body. While these cells do not possess a definite cell membrane, there is a condensation of the cytoplasm at the periphery of the cell by which a protoplasmic membrane is formed. However, peculiar to nerve cells are the processes that are given off from the cell body, some of which, axons of motor cells, are extremely elongated, extending three feet or more. The nucleus and cytoplasm also possess certain other structures peculiar to nerve cells.

The nuclei of nerve cells are large, round and possess a sharply defined nuclear membrane which encloses a fluid nucleoplasm *(karyoplasm),* a network of fine linin fibers, a small amount of chromatin and a large nucleolus. Not infrequently two nucleoli are present. The scant amount of chromatin gives the nucleus a vesicular appearance. It varies somewhat with the size of the cell, being most abundant in the smaller cells where it forms a delicate network. In the larger cells the chromatin consists of a few scattered, granular masses. The nucleus, which stains lightly with basophilic stains, is usually located in the central portion of the cell, however, an exception to this is to be found in the cells of Clark's column in the spinal cord, where the nuclei occupy an eccentric position.

The cytoplasm which is often referred to as the *perifibrillar substance* or *neuroplasm*, contains a number of structures: *neurofibrillae*, *Nissl granules (tigroid bodies* or *chromophil substance)*, *inclusions* which are principally fat droplets and pigment granules, *mitochondria*, and a *Golgi apparatus*. Since it is impossible to show all of these structures with any single stain, it necessitates the use of several sections employing different methods, if a complete picture and understanding of these cells is to be gained.

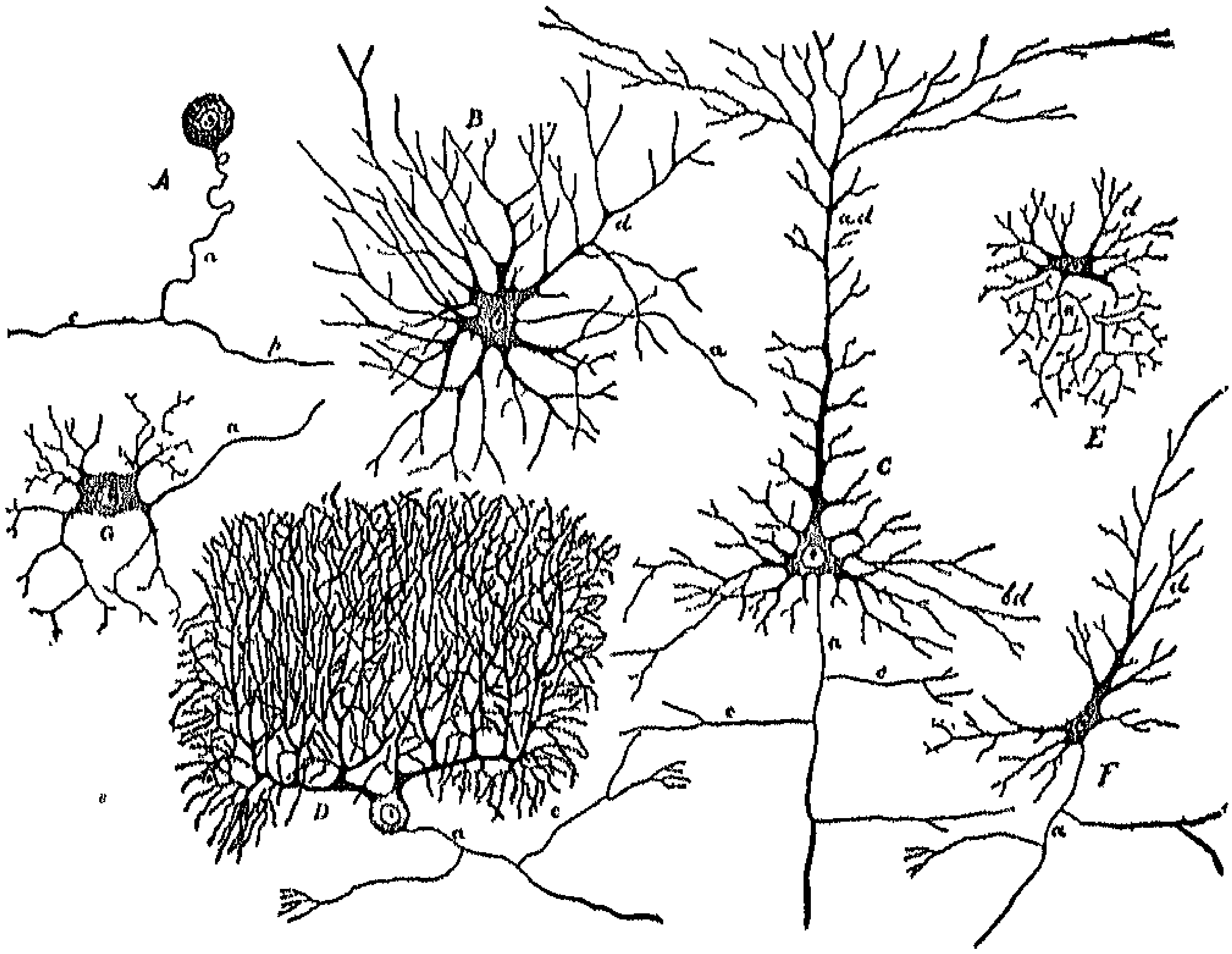


FIG. 64. Various forms of neurons of the human nervous system. The sheaths are not shown. The dendrites and a portion of the axons are shown. *(A)* From spinal ganglion. *(B)* From anterior horn of spinal cord. *(C)* Pyramidal cell from cerebral cortex. *(D)* Purkinje cell from cerebellar cortex. *(E)* Golgi cell of type II from spinal cord. *(F)* Fusiform cell from cerebral cortex. *(G)* Sympathetic ganglion cell. *(a)* Axon. *(d)* Dendrites. *(c)* Collateral branches. *(ad)* Apical dendrites, axial stem shorter than normal. *(bd)* Basal dendrites. *(p)* Peripheral process. (Courtesy, J. Parsons Schaeffer, Ed.: "Morris' Human Anatomy," Philadelphia, The Blakiston Company.)

Neurofibrillae are delicate threadlike fibers which are found in the cytoplasm of the body of the nerve cell and extend throughout the entire extent of its processes. If sections stained by Cajal's silver method are examined, the neurofibrillae are seen to form a closely meshed network of branching and anastomosing fibers within the cell body. However, on entering the processes, the fibers straighten out and lie parallel to one another and to the long axis of the process. The exact function of these fibrillae is not known.

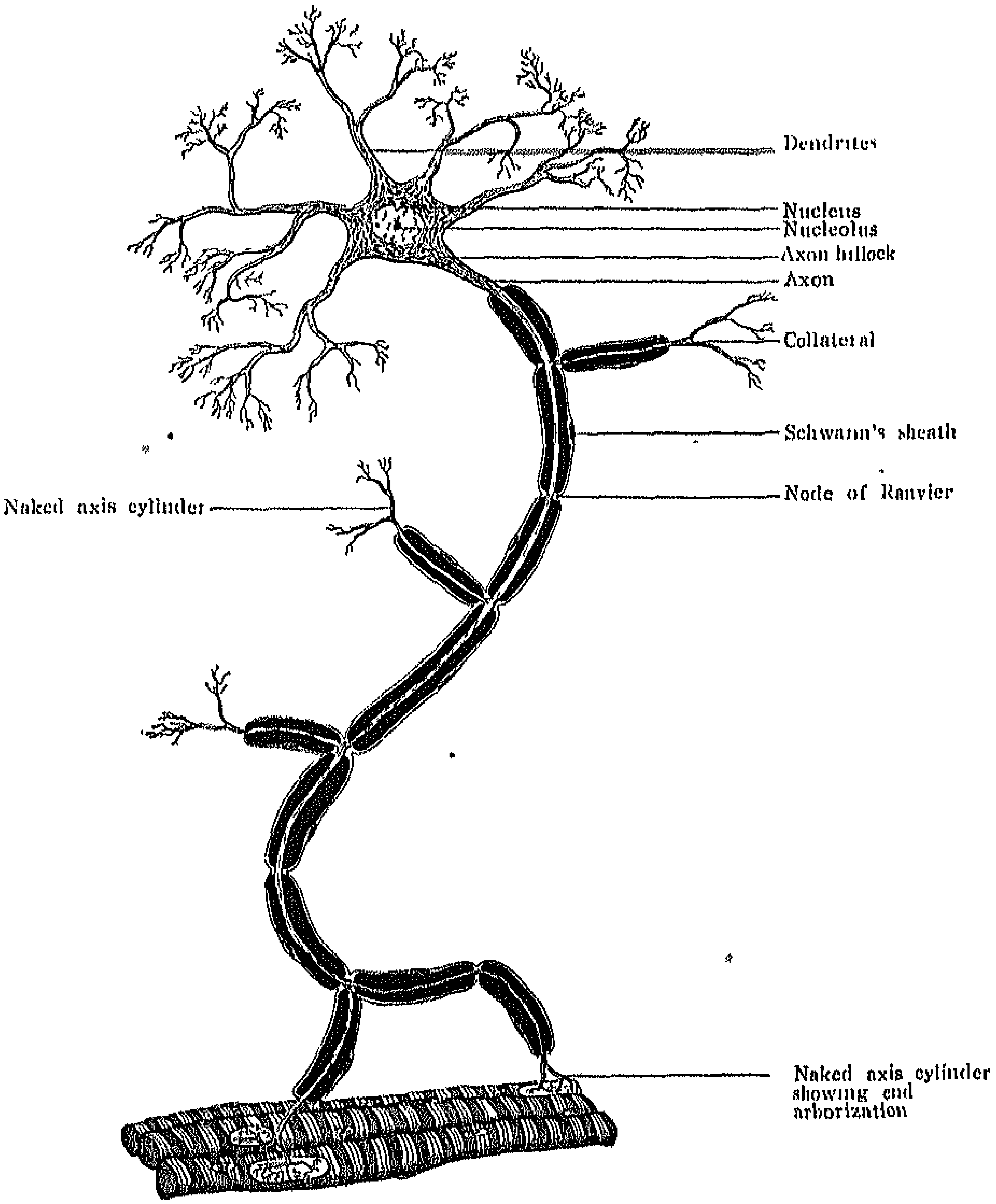


FIG. 65. Diagram of a peripheral myelinated nerve fiber.

The cytoplasm also contains a substance in the form of small granules which are aggregated in flattened, irregular masses *(Nissl bodies)*, which react intensely to the basic dyes. Since the staining reaction of these bodies is similar to that of chromatin it is called *chromophil substance*. Because of the spotted appearance they give to the cells, Nissl bodies are sometimes referred to as *tigroid bodies*. So we find the terms, Nissl bodies, chromophil substance, and tigroid bodies, all refer to the same granulation substance in the cytoplasm. These bodies are found in the cytoplasm of the cell body and in the dendrites of all nerve cells, but they are not found in the axon hillocks or in the axons.

The number and arrangement of the Nissl bodies vary considerably according to the locality and size of the cell in which they occur. They

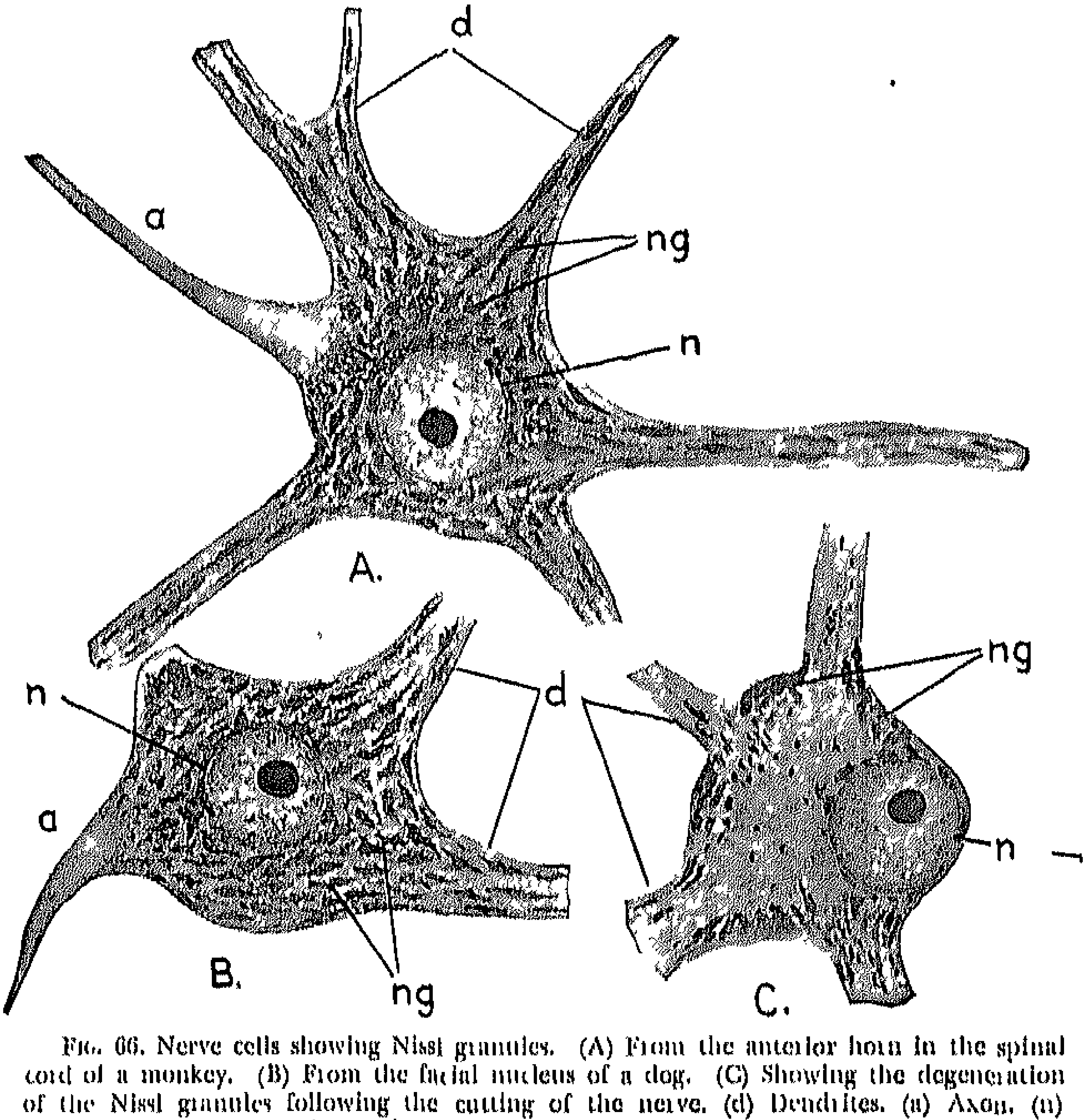


FIG. 66. Nerve cells showing Nissl granules. (A) From the anterior horn in the spinal cord of a monkey. (B) From the facial nucleus of a dog. (C) Showing the degeneration of the Nissl granules following the cutting of the nerve. (d) Dendrites. (a) Axon. (n) Nucleus. (ng) Nissl granules. (After Schäfer.)

are largest and most abundant in the larger cells. Chromophil granules are not present in the form of aggregations in the smallest nerve cells, although the color of their cytoplasm, when stained with the proper dyes, suggests that this substance may be present in a diffuse form. The arrangement of the Nissl bodies presents the same pattern in cells of a given type; this has led to the belief by some that the locality or function of the cell can be identified, within limits, by the pattern which these bodies assume.

The function of the chromophil substance is not clearly understood, although it has been suggested that it is related to the nutritive processes of the cell (reserve store of food for the nerve cell). Injury or disease of the nerve cell is quickly reflected by the Nissl bodies. When the cell has been subjected to the effects of poisons, or injury, the Nissl bodies break down, their substance being diffused through the cytoplasm, a condition known as *chromatolysis.* However, some normal neurons have the appearance of chromatolysis as in the cells of Clark's column. Chromatolysis also takes place in nerve cells after their processes have been cut. By sectioning nerve fibers and noting the cells in the brain and spinal cord in which this change has occurred, it is possible to identify the location of the cells from which the injured fibers take their origin.

The inclusions found in nerve cells are principally fat droplets and pigment granules. Granules of melanin, a deep brown pigment, are found in some nerve cells, but its purpose in these cells is not known.

Other structures found in nerve cells, and not understood, are the mitochondria. They are found throughout the neuroplasm of the cell body and its processes, and exist in the form of granules or rods.

The Golgi apparatus can be demonstrated in all nerve cells. Its form varies from a small, single granule *(Golgi body)* to a complex coarse meshwork. While it is ordinarily restricted to the cell body, it may extend into the dendrites. It may be arranged diffusely throughout the cell or it may form a ringlike structure around the nucleus.

Centrosomes are absent, or if present, are atypical. The absence of centrosomes is probably related to the inability of nerve cells to reproduce by division. There is no replacement of the cells in nervous tissue once they have been destroyed.

The characteristic feature of a nerve cell is its processes. These are extensions of the cytoplasm which, in some cases, continue for a considerable distance from the body of the cell. The processes of a nerve cell are of two kinds: *dendrites* and *axons.*

The dendrites are broad at the place where they leave the cell, but gradually taper to a point. They branch profusely, the branches appearing shortly after the process leaves the cell body. Swellings or varicosities occur on the branches of many dendrites. These are frequently angular and give the dendrite a thorny appearance. The cytoplasm of the cell is continued into the dendrites without modification, while the neurofibrillae extend to the ends of the smallest branches. The Nissl bodies become elongated and rodlike, as they are continued into the processes.

While a cell may have a number of dendrites, as a rule it has only one axon. In unipolar cells, however, this axon divides shortly after leaving the body of the cell to form two axones. In exceptional cases, two axons may arise from a single cell, or the axon may spring from the root of a dendrite. Axons may arise either directly from the cell body, from the root of a dendrite or from a slightly projecting mass of differentiated protoplasm known as the *axon hillock* or *implantation cone*. The latter is by far the most common origin. Axons arising from an axon hillock maintain a constant diameter throughout their course except for a slight constriction at the point where they attach to the axon hillock. Axons give off branches *(collaterals)* a short distance from the cell body. These collaterals are not as numerous as the branches of the dendrites, but they occur at regular intervals and arise from the stem of the axon at right angles. Axons and their branches end in a tuft of naked fibrils which form *end arborizations* or *telodendria*. The length of an axon depends on the location and functional character of its cells. In some cases it proceeds only a short distance from the cell while in other cases it is a process of considerable length. This can best be appreciated when it is recalled that the axons of

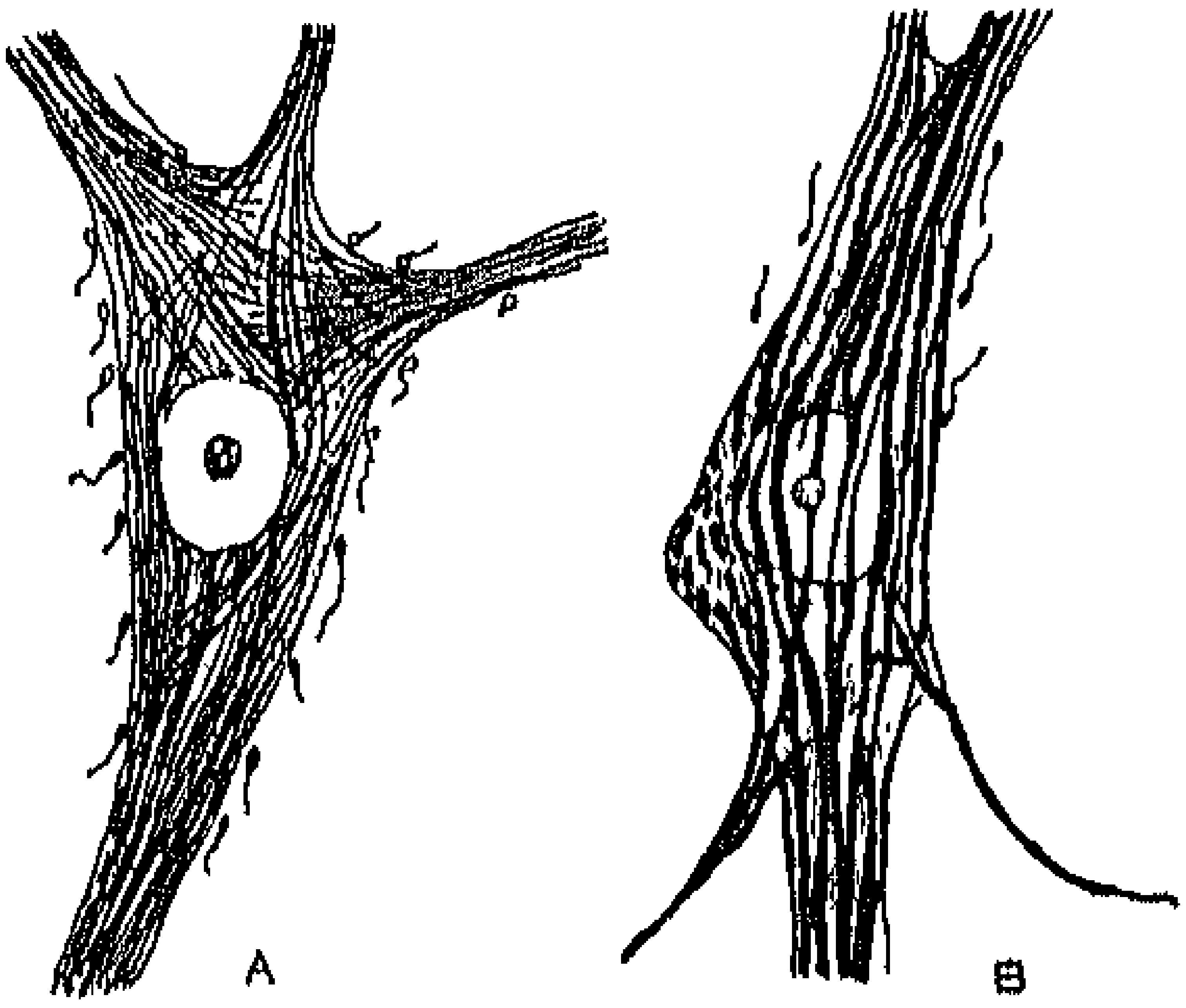


FIG. 67. Neurofibrils during activity (A) and during hibernation (B). (After Cajal, 1906.) (Courtesy, Penfield: "Cytology and Cellular Pathology of the Nervous System," New York, Paul B. Hoeber, Inc.)

nerve cells in the sacral segments of the spinal cord extend to the extremities of the foot.

Morphologically the axon differs in several respects from the cytoplasm of the cell from which it arises. Unlike the cytoplasm it does not contain Nissl granules, or a Golgi apparatus. It does contain mitochondria and neurofibrillae; the latter pass through the neuroplasm of the axon hillock and continue unmodified in the structure of the axon.

NERVE FIBERS

The nerves which pass from the brain *(cranial nerves)* and spinal cord *(spinal nerves)* to the peripheral structures of the body, consist of numerous fibers *(nerve fibers)* which are bound together in bundles *(funiculi)*. There are two kinds of nerve fibers in the nervous system, *myelinated* and *unmyelinated*. Myelinated fibers occur in the brain, the spinal cord and their peripheral branches. Structurally the myelinated fibers in the central nervous system are not exactly like the myelinated peripheral fibers. In the central nervous system the fibers lack a neurilemma sheath, which is present in the peripheral myelinated fibers. Unmyelinated fibers are associated with the autonomic nervous system and are present in the peripheral nerves (pain fibers). Numerous naked axons are also found in the gray matter of the brain and spinal cord.

The classification of nerve fibers as myelinated or unmyelinated can be further subdivided so that there are in the nervous system four kinds of nerve fibers: 1. Myelinated nerve fibers having a neurilemma sheath. These are found in the cerebrospinal nerves of the peripheral nervous system. 2. Myelinated nerve fibers without a neurilemma sheath, sheath cells, or nodes of Ranvier. These fibers are restricted to the brain and spinal cord. 3. Unmyelinated fibers with a membrane similar to a neurilemma. These are called Remak's fibers and are found in the autonomic system and in the cerebrospinal nerves (fibers receiving pain stimuli). 4. Bare axons, which are found in the central nervous system.

1. MYELINATED PERIPHERAL NERVE FIBERS. These myelinated nerve fibers consist of a central core, the *axis cylinder,* which is enclosed in a relatively thick layer of fatty material supported by a reticulum, the *myelin sheath.* External to, and surrounding the myelin sheath is a thin, transparent membrane, the *neurilemma (Schwann's sheath).* Myelinated fibers are extremely variable in size, ranging from 2–20 microns in diameter.

The axis cylinder is the continuation of the axon of the nerve cell into the fiber. It consists of a semifluid substance *(neuroplasm; axoplasm)* in which are embedded a number of neurofibrillae. The

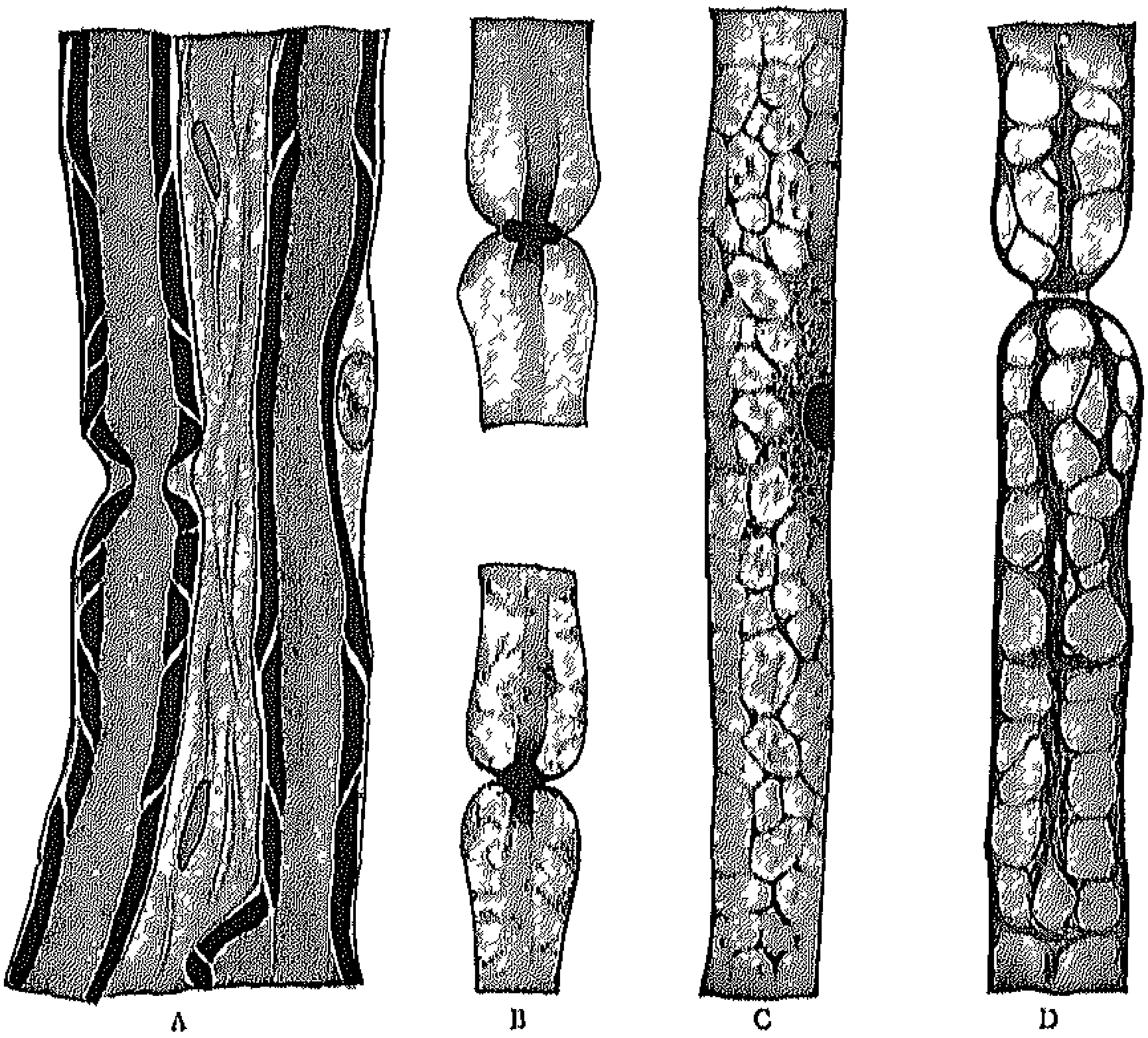


Fig. 68 Nerve fibers with myelin sheath. (A) Osmic acid preparation, frog. (B) Silver nitrate, guinea pig (after Schäfer and below after von Möllendorff). (C) Methylene blue, cat (after Nemiloff). (D) Silver impregnation, cat. (Cajal.) (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

neurofibrillae in the axis cylinder are continuous with those which are present in the nerve cell, and which are regarded as the structures by which nerve impulses are transmitted. They continue the entire length of the nerve fiber and are lost in its end arborization. The substance of the axis cylinder is enclosed by an extremely delicate membrane, the *axolemma.*

The myelin sheath is a semifluid combination of fats and lipoids supported by a reticular framework of *neurokeratin.* Myelin is considered to function as an insulating material to prevent the spread of nerve impulses from one fiber to a neighboring fiber. In the fresh condition the myelin gives the fiber a white glistening appearance. It makes its appearance shortly after the axis cylinder leaves the nerve cell, and continues almost to the point where the fibers branch to form the end arborization. In properly prepared sections, the reticulum can be seen as delicate bars of modified protoplasmic material, called neurokeratin, forming a framework supporting the substance of the myelin sheath. It is possible that this reticulum may be a coagulation product which is produced by fixation. Owing to its lipoid character, myelin is dissolved by some of the reagents employed in the preparation of sections, however, it is readily demonstrated by methods which permit the application of osmic acid. Myelin is stained black by the acid, while the axis cylinder appears as a lighter band in the middle of the fiber. In these osmic stained sections, narrow clefts appear in parts of the thickened reticulum and correspond to the *incisures of Schmidt-Lanterman.* These narrow clefts extend obliquely through the myelin substance and are irregularly spaced. There is evidence that neurokeratin, incisures, etc., do not exist in living tissues.

The myelin sheath is not continuous, but is divided into segments by a series of constrictions, the *nodes of Ranvier.* These nodes occur at regular intervals, the segments being shorter in the smaller fibers and longer in the larger fibers; they are always present where fibers branch.

The neurilemma, or sheath of Schwann, is a thin, transparent membrane which forms the external investment of the nerve fiber. It lies upon the myelin sheath. It is not interrupted at the nodes of Ranvier, but dips down between the segments of the myelin sheath where it lies upon the axis cylinder. The part of the fiber lying between two nodes is called an *internodal segment.* A single nucleus *(neurilemma nucleus)* surrounded by a small accumulation of granular protoplasm lies immediately beneath the neurilemma of each internodal segment. Thus, each internodal portion of the neurilemma is regarded as representing the product of a single sheath cell of ectodermal origin (neurilemma cell of Schwann). Mitochondria and a Golgi apparatus have been demonstrated in the cytoplasm surrounding the nuclei.

In the peripheral nerves, fibers from the surrounding connective tissues are closely applied to the surface of the neurilemma in the form of a delicate membrane, known as the *sheath of Key and Retzius.*

As seen in cross section the nerve fibers in ordinary preparations appear as circles, the central portions of which are occupied by the axis cylinders, their circumferences being outlined by the neurilemma. The clear space between the axis cylinder and the neurilemma, in each fiber, is occupied in freshly obtained nerves by the myelin sheath, the substance of which has been removed by the reagents employed in preparing the section.

The neurilemma arises from the crest-cells of the neural plate in the embryo, therefore, it is not present in nerve fibers within the brain and spinal cord. It is applied to the fiber as it emerges from the central area and continues its entire length without interruption. The neurilemma extends a little beyond the myelin sheath, where both end before the fiber breaks up into the branches which form the end arborization.

In sensory fibers the neurilemma ceases as the fibers enter the central structures, its place being taken in the brain and spinal cord by an interlacing of the processes of the glia fibers, which is applied to the surface of the myelin sheath.

2. MYELINATED FIBERS OF THE CENTRAL NERVOUS SYSTEM. Myelinated nerve fibers of the brain and cord differ slightly in structure from myelinated peripheral fibers. The former have no neurilemma sheaths, sheath cells, or nodes of Ranvier.

3–4. UNMYELINATED NERVE FIBERS. There are two kinds *of unmyelinated fibers: Remak's fibers and naked axons. The axis* cylinder of an unmyelinated fiber consists of a number of neurofibrillae, surrounded by a perifibrillar exoplasm. The myelin sheath is absent, the axis cylinder being invested by a delicate membrane corresponding to the neurilemma of myelinated fibers. This membrane is separated from the axis cylinder by a thin layer of protoplasm. There are no constrictions of the investing structures of the fiber to form nodes, but flattened, oval nuclei occur at regular intervals beneath the neurilemma, which marks a division into the cells of Schwann. The axis cylinders of unmyelinated fibers may branch, the branches passing, in extensions of the neurilemma, to adjacent bundles of fibers.

The axis cylinders of unmyelinated nerve fibers are formed by processes from the cells of the autonomic system. Owing to their small size, and the similarity of their appearance to the bundles of the con*nective tissue by which they are surrounded, they are difficult to* identify in ordinary preparations. Bundles of unmyelinated fibers can be distinguished in relation to groups of ganglion cells in the walls of the alimentary canal and in similar relations to other structures (salivary glands). They can also be detected in the form of small, sharply defined dots between the myelinated fibers in cross sections of the peripheral nerves.

Some unmyelinated fibers originating in the autonomic system extend through the gray communicating rami and join the peripheral nerves. These fibers are known as the fibers of Remak.

Naked axons, devoid of any sheath, are found in abundance in the gray matter of the brain and spinal cord.

DEGENERATION AND REGENERATION OF NERVES

A close relationship exists between the axon and the myelin sheath. Following injury to a peripheral nerve fiber, there is a rapid degeneration of both the myelin sheath and the enclosed axon of the fiber distal to the injury. Proximally the degeneration usually extends along the fiber only as far as the node of Ranvier nearest the point of injury. Chemical changes occur in the myelin and it breaks into globules of lipoidal material of varying sizes. The axon fragments into small granular appearing masses. This disintegration of the nerve fiber is

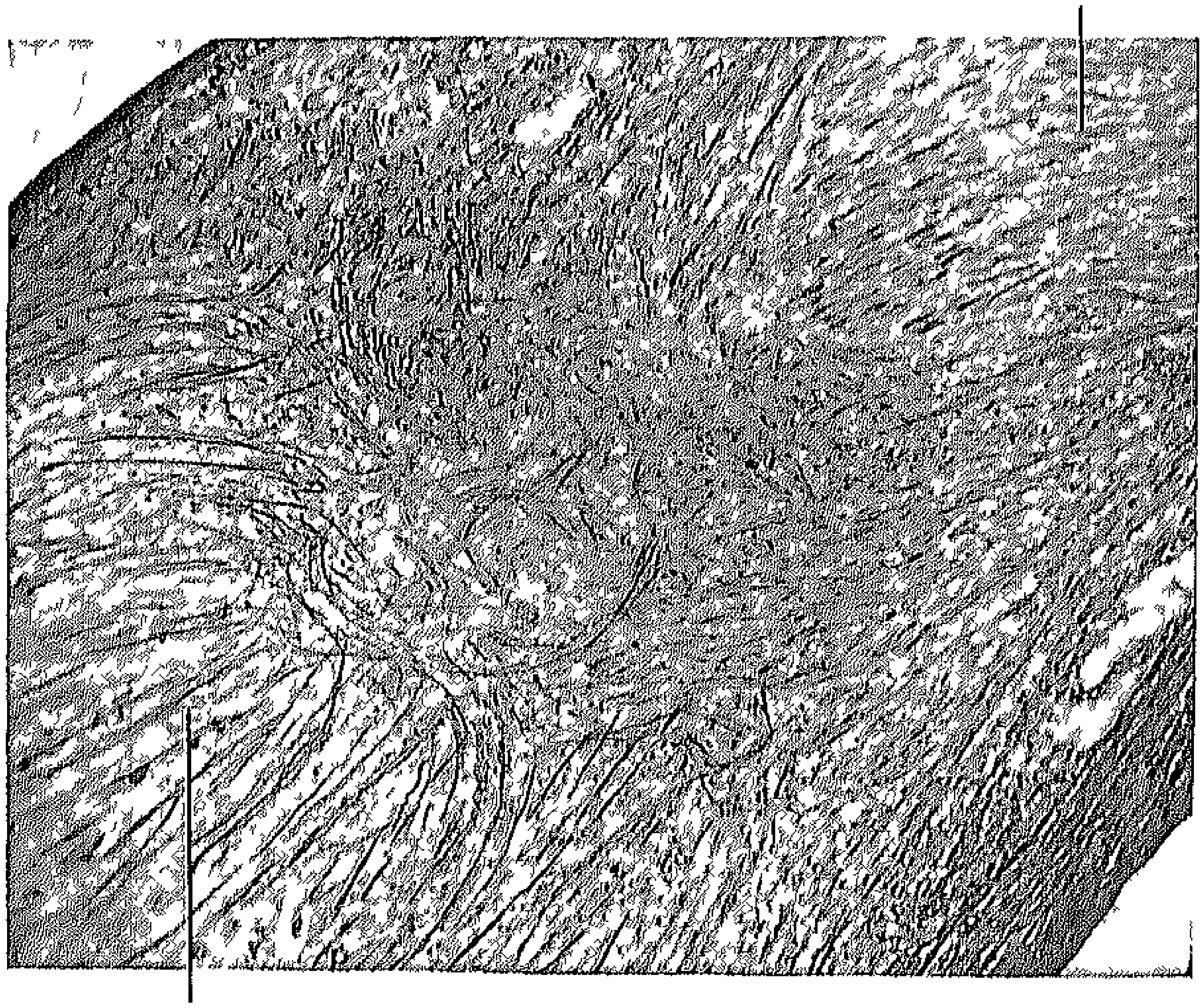


FIG. 69. Neuroma. Cut sciatic nerve of rat. Note club endings of fibers growing into peripheral stump and tangled arrangement of fibers in space between the two cut ends of the nerve. Photomicrograph.

called *Wallerian degeneration.* After injury of the nerve fiber, the cells of the neurilemma sheath of the degenerating segments of the fiber undergo hyperplasia and join end to end to form so-called band fibers which are the essential elements in the regeneration of the injured nerve fibers. The nerve fibers of the central nervous system, which are devoid of neurilemma sheaths, are also incapable of regeneration.

In the regeneration of cut or injured nerve fibers, the axons grow out from the central end of the degenerated nerve. This outgrowth is not orderly, but the fibers grow in all directions. If the gap between the two ends of the damaged nerve is not very great, the growing axons will cross the space and contact the distal cut end of the degenerated nerve. If this is accomplished, the enlarged, growing end of the axon follows along the band fibers to the terminal part of the nerve. These band fibers not only give support and guide the growing axons, but they also give rise to the new neurilemma sheaths of the regenerating nerve fibers.

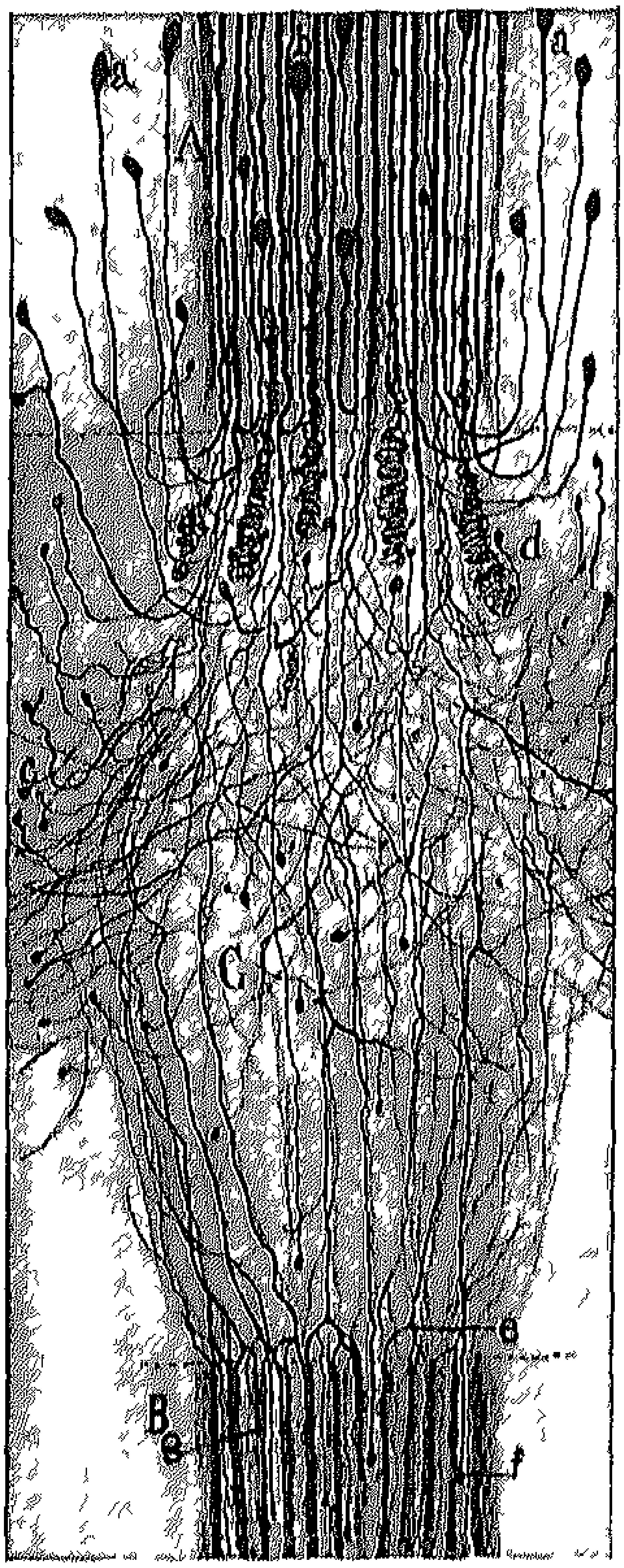


FIG. 70. Diagrammatic drawing of a regenerating nerve. (A) Central stump. (B) Distal stump. (C) Interval between stumps. (a, b) Bulbs on the ends of fibers growing centrally in and around the central stump. (f, g) Bulbs on the ends of fibers growing into the distal stump. (c) Bulb on the end of a fiber in the scar. (d) Coil formed by centrally growing fiber. (Cajal.) (From Ranson: "Anatomy of the Nervous System," 7th ed., Philadelphia, W. B. Saunders Co.)

The Synapse

The question of the exact histological relationship that exists between two neurons in a reflex chain is still unsettled. The view held by the greater number of investigators is that there is no anatomical connection between one neuron and another. The fibers which form the end arborizations of a sensory neuron, for instance, appear to wind about the fibers which form the telodendria (terminal processes) of the dendrites, without protoplasmic continuity of the two. The fibers, however, form contacts with one another by means of which the impulses they transmit may pass from the sensory to the motor neuron. This association of the end-processes of two neurons is called a *synapse.*

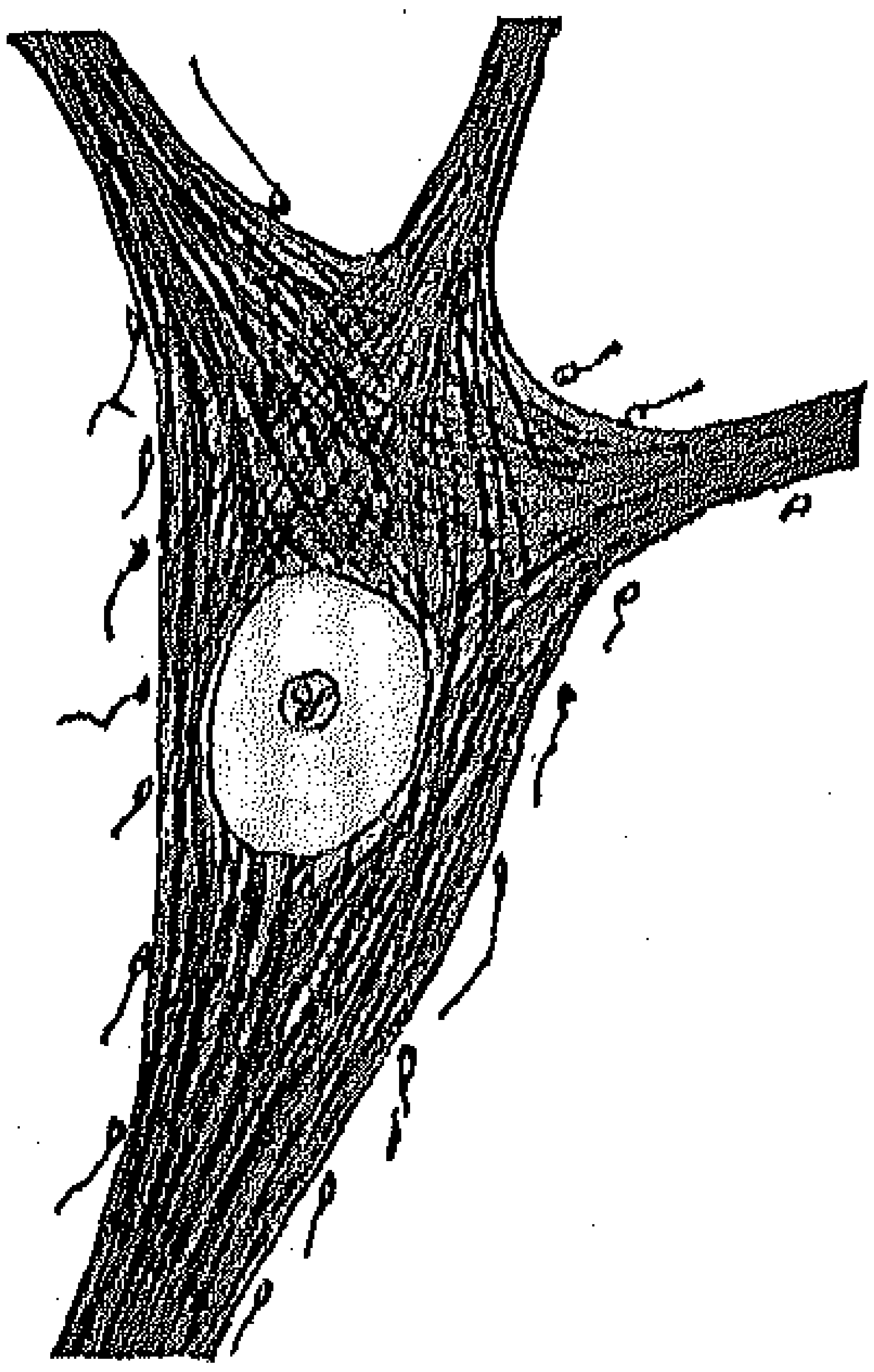
According to Bodian, in properly prepared and stained material it is possible to demonstrate the discontinuity of protoplasm at the synapse. A definite membranous barrier exists and is called a *synaptic membrane* or *synaptolemma.* While it has not yet been possible to demonstrate this synaptic membrane in all areas (olfactory axodendritic synapse among others) it is likely that when adequately prepared sections are studied they will be found. In those synapses where a synaptic membrane is present, the neurofibrillae of one neuron do not extend across the membrane into the second neuron. Another bit of evidence in support of the idea of protoplasmic discontinuity at the synaptic junction, is the work of Hoff, 1932. He sectioned the axons of nerve cells whose terminal boutons were in synaptic relation with neurons in the spinal cord. These boutons degenerated, thereby indicating that they were dependent for their nutrition on the axon alone.

In some of the lower animals an actual continuity of the protoplasm from the axon of one nerve cell to the dendrites of another, has been demonstrated. Although it has been assumed by some that such a connection exists in the nervous system of the higher animals, the assumption is not supported by clear anatomical evidence.

Two types of synaptic relationship may be recognized in the nervous system: 1. *Axodendritic* synapse, where the end arborizations of an axon may be in contact with those of a dendrite of another neuron. 2. An *axosomatic* synapse, where the synapse occurs between the end arborizations of the axon of one neuron with the cell body of another.

In connection with the synapse, mention should be made of the types of neuron junctions. The most common type is the *bouton.* These occur as swellings on the axon terminals and may be in relation to the cell body or the dendrite of another neuron. *Club endings* on the other hand, occur on large fibers where the diameter of the fiber is great enough that terminal enlargement is unnecessary since it is doubtful if it would facilitate transmission of the impulse. *Gemmules* are another type. These are short spinelike processes of the dendrites and are only found in synapses between dendrites and axons. Synaptic junctions may occur by *apposition* between an axon and a dendrite that run parallel to one another, an axon and cell body, or occasionally between two parallel axons where the second axon is unmyelinated.

NERVE IMPULSE TRANSMISSION. Very little is known about what actually happens when an impulse is transmitted through the neuron. Moreover, it is not known what part the structural constituents of the neuron play in the actual conduction of the impulse. But if any of the constituents are associated with this phenomena, we can probably narrow it down to either the neuroplasm, neurofibrillae, or the surface membrane of the neuron. We know that the myelin sheath and the neurilemma are not essential, since naked neurons can and do transmit impulses.



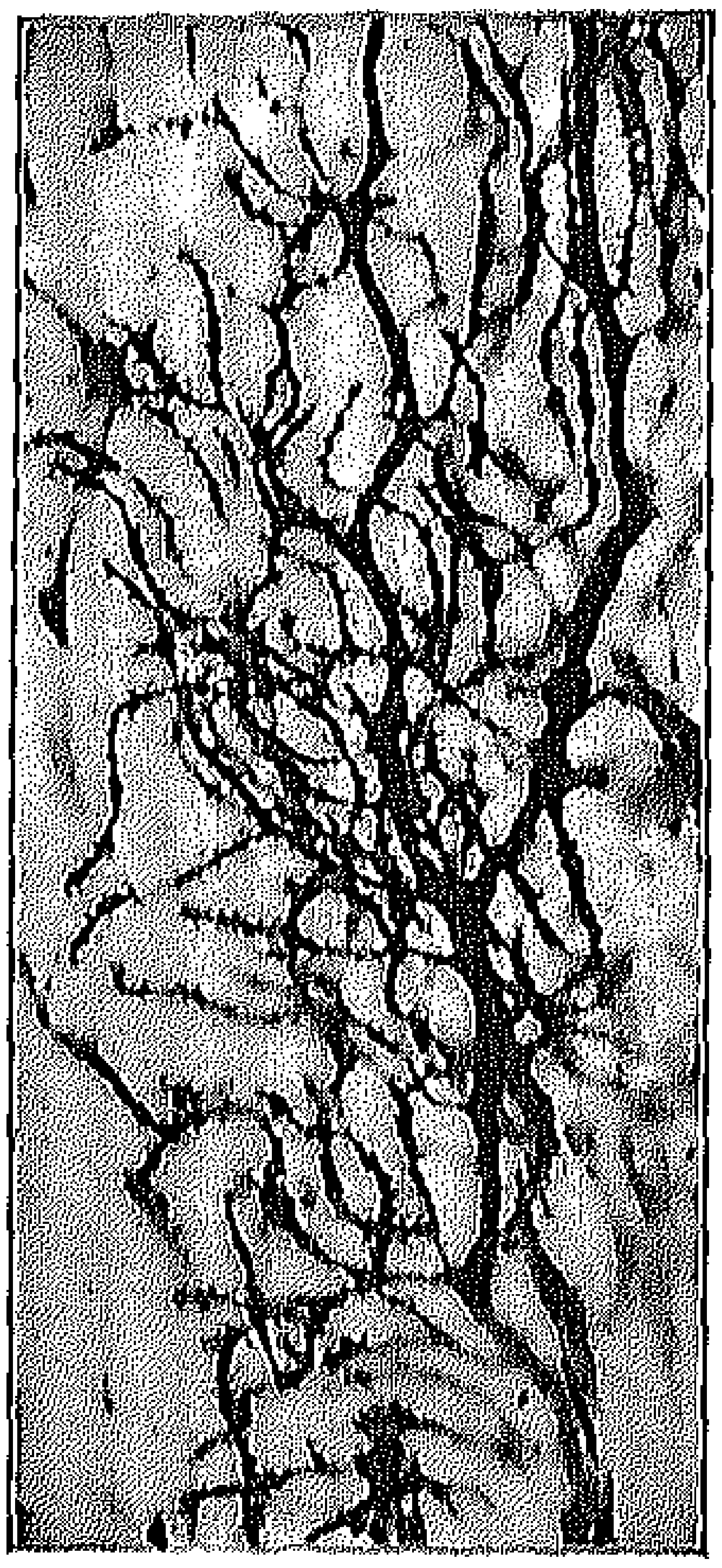


Fig. 71. *(Left)* Nerve cell showing bouton type of synaptic ending. (Cajal.) (From Ranson: "Anatomy of the Nervous System," 7th ed., Philadelphia, W. B. Saunders Co.)

Fig. 72 *(Right)* Purkinje cell arborization to show gemmule type of synaptic ending. Chrome-silver method of Golgi. Photograph. (Courtesy, Smith and Copenhaver: "Bailey's Text-book of Histology," Baltimore, The Williams & Wilkins Co.)

Concerning the physiological changes in the nerve cell during the impulse transmission, a few things are known. Oxygen is consumed, with the formation of carbon dioxide and the production of heat.

There is also an electrical change which accompanies the transmission of the impulse. This change in electrical potential is measurable and is correlated with function and size of the nerve fiber. This characteristic makes it possible to analyze the constituents of a peripheral nerve and to determine the individual types of fibers composing it. Rates of conduction can be measured and they range from 1–75 meters per second.

While there is a definite "electrical factor" accompanying the transmission of nerve impulses along the fiber, we also know that certain changes (chemical) take place at the synapse. At the parasympathetic and somatic efferent terminations and at the synapse occurring in the sympathetic ganglia, acetylcholine is released by the impulse transmission, while activation of the sympathetic fibers produces adrenine at the terminal points. Recent research has shown that acetylcholine and adrenine are also present within the substance of the fibers themselves, the former being limited to fibers of the sympathetic system while the adrenine is restricted to the parasympathetic fibers. Within the substance of the fibers these chemicals are thought to participate probably in the production of the impulse.

These two phenomena of neuron activity have led to the formation of two schools of thought: one group credits the electrical change as

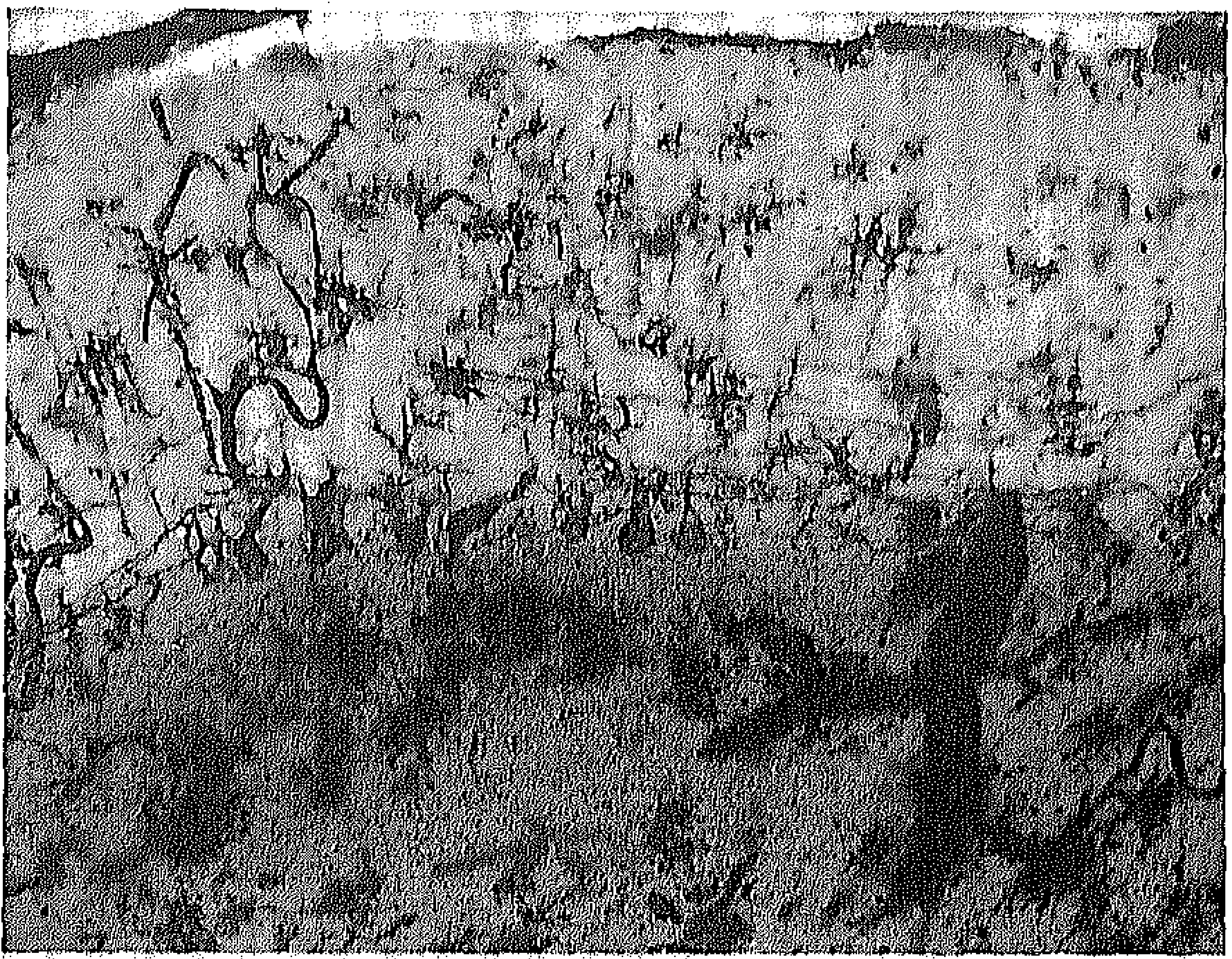


FIG. 78. Branches of axons of basket cells in relation to the cell bodies of Purkinje cells illustrating parallel axo-somatic type of synapse. Silver stain. Photomicrograph.

being the factor which results in impulse transmission, while the other group credits the chemical substance with the power to produce the impulse. Probably when the problem is finally solved, both the change in potential and the formation of these chemical substances will be found to contribute to impulse transmission.

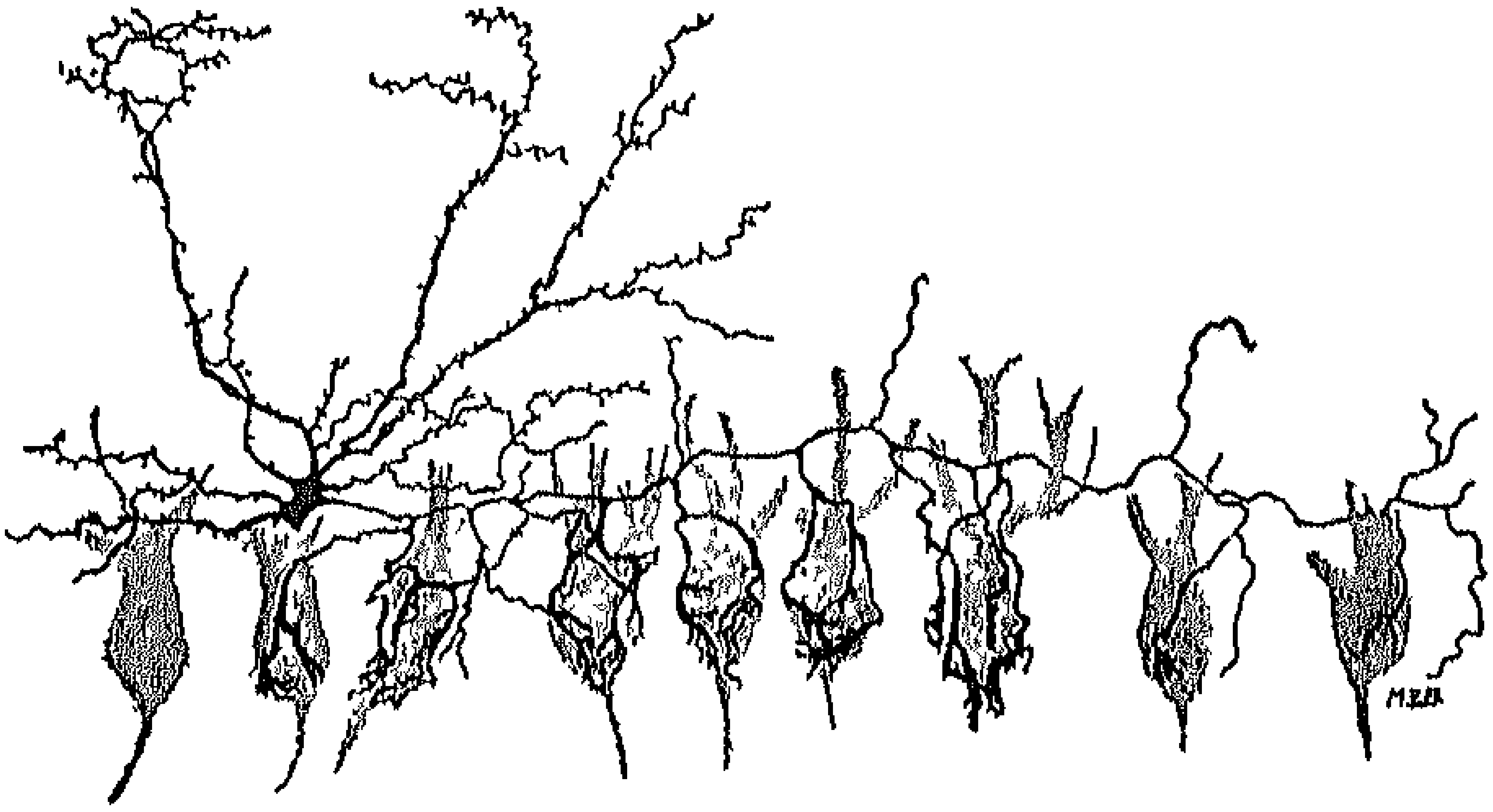


FIG. 74 Diagrammatic representation of parallel axo-somatic synapses involving cell bodies of Purkinje cells and branches of the axon of a single basket cell. Method of Golgi (Cajal) (From Ranson: "Anatomy of the Nervous System," 7th ed., Philadelphia, W. B. Saunders Co.)

NERVE TRUNKS

A nerve trunk (peripheral nerve as seen in gross dissection) consists of cords or bundles *(funiculi)* of nerve fibers enclosed by a compact arrangement of connective tissue (the *perineurium*). The funiculi are bound together by loosely arranged connective tissue (the *epineurium*). In the fresh condition, the funiculi have a glistening appearance, since they consist, for the most part, of myelinated fibers. Bundles of unmyelinated fibers appear a dull gray. In the brain and spinal cord, the fibers lie parallel to one another and pursue a nearly straight course. In the funiculi of the peripheral nerves, the fibers follow an irregular, wavy course so that, in sections, they are cut transversely, obliquely and to some extent, longitudinally. This is evidently for the protection of the fiber when the nerve is stretched. Connective tissue fibers derived from mesoderm, extend from the perineurium and form a delicate investment for the nerve fibers, the *endoneurium*. The connective tissue of the endoneurium forms septa by which the nerve fibers are separated into bundles, and it is also condensed on the surface of the neurilemma, where it becomes the sheath of Henle.

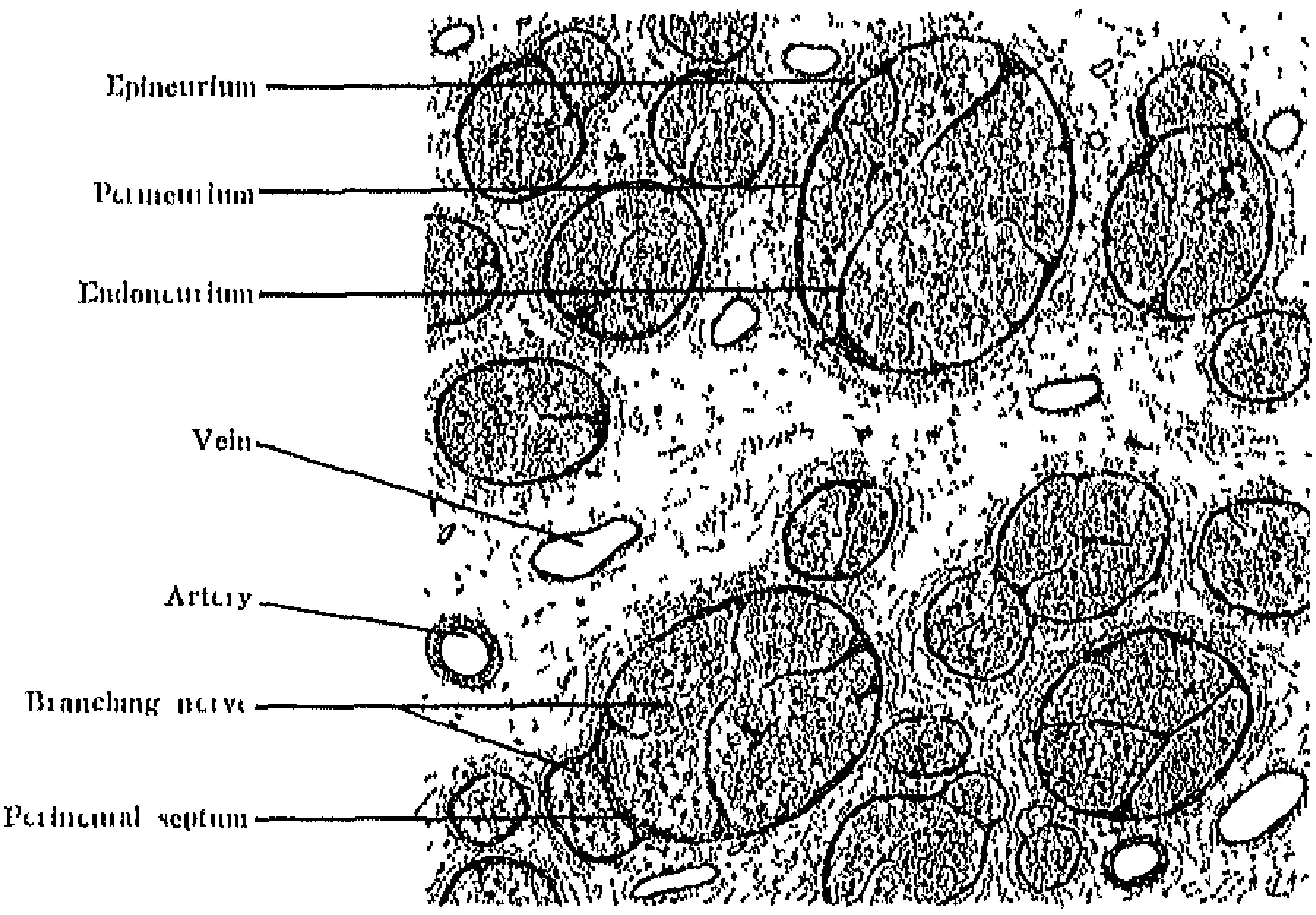


FIG. 75. Portion of a cross section through the sciatic nerve of a newborn.

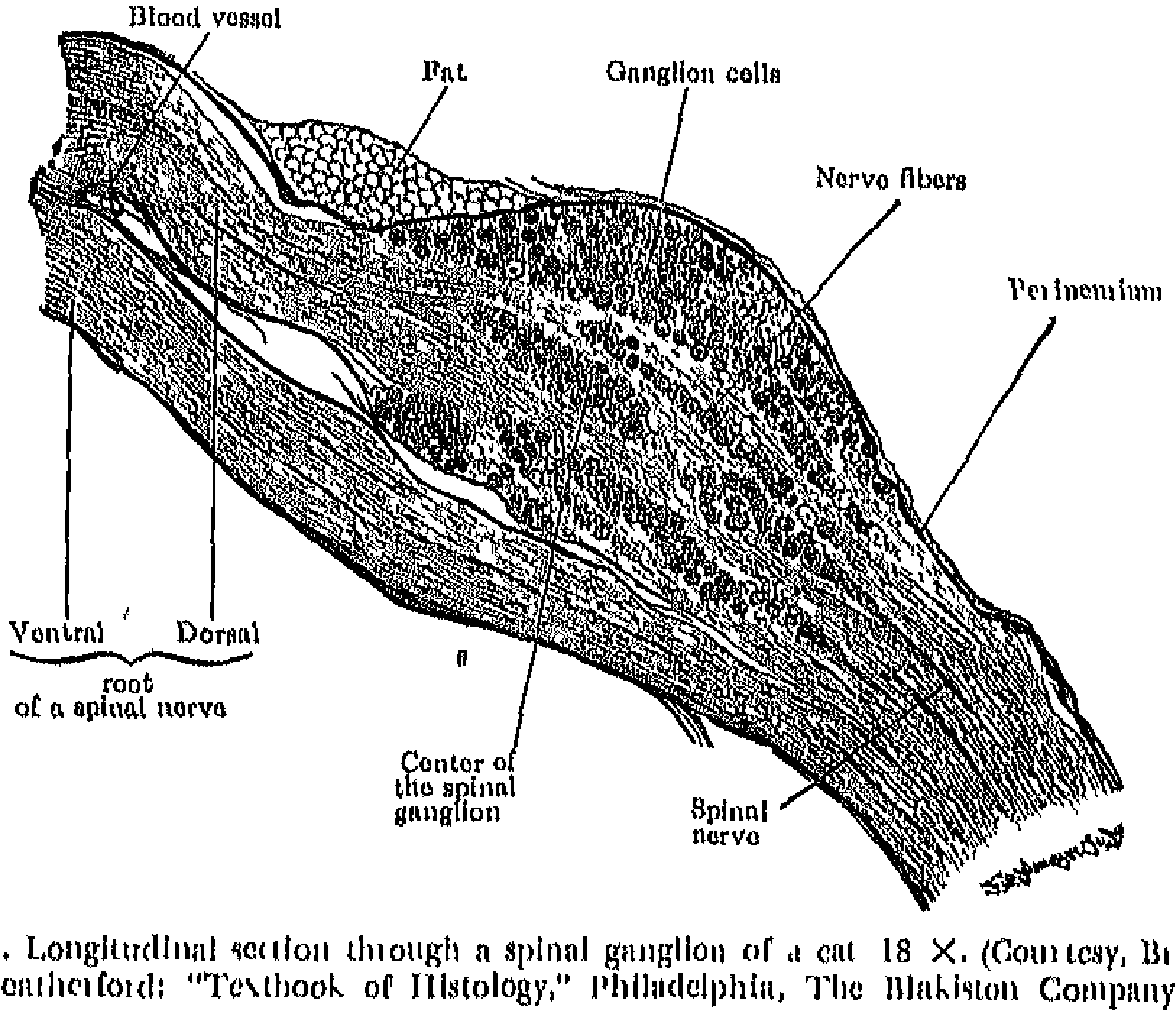


FIG. 76. Longitudinal section through a spinal ganglion of a cat 18 ×. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

A partitionlike extension of the perineurium may be seen in some instances to cross the funiculus. This indicates where the division of the nerves into branches is taking place. As the nerve trunk continues, it diminishes in size through a reduction of the epineurium, which finally disappears; the branches of the nerve consisting of single funiculi, each surrounded by perineurium. Each of these branches finally breaks up into its constituent fibers, the only connective tissue investment of which is Henle's sheath. The nerve fiber ultimately loses its myelin sheath and neurilemma, and divides into a number of threadlike branches *(end arborizations)*, which end in relation to sensory, or motor structures.

GANGLIA

SPINAL GANGLIA. On the dorsal root of spinal nerves is an enlargement or ganglia which contains the cell bodies of the sensory neurons. The bundle of nerve fibers which is separate from the ganglionic portion, contains fibers of the ventral root (motor fibers) which join with the fibers of the dorsal root (sensory fibers) to form the peripheral nerve. The connective tissue of the peripheral nerve (perineurium and epineurium) continues over the ganglia in the form of a connective tissue capsule. Trabeculae extend into the ganglia to form a supporting framework, to enclose the ganglion cells.

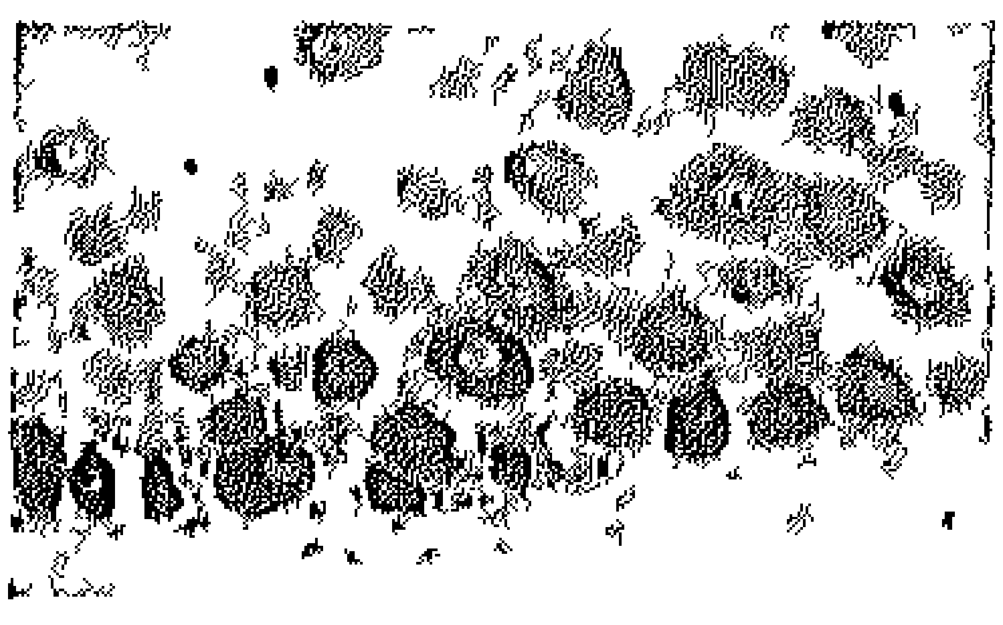


FIG. 77. Cells of dorsal root ganglion Photomicrograph

The spinal ganglion cell is unipolar. The body of the cell is approximately round and varies in size from 15–100 microns. After leaving the cell body, the axon twists back on itself and forms a series of loops near the cell body. This arrangement of the axon is known as the *glomerulus*. After forming the glomerulus, the axon branches; one branch is directed peripherally, the other is directed toward the cord. The cytoplasm of these ganglion cells is finely granular, the nucleus is large and vesicular, each containing a fine chromatin network and a deeply stained nucleolus. Flattened cells with prominent nuclei *(mantle* or *satellite cells)* form a capsule of membranous sheath investing each ganglion cell. These mantle cells, which are continuous with the neurilemma sheath of the corresponding nerve, are derived from the ectoderm of the neural crest.

AUTONOMIC GANGLION. The cells of the autonomic ganglia are practically all multipolar. The cell bodies range in size from 20–45 microns. Like the spinal ganglion cell, these cells have large, round,

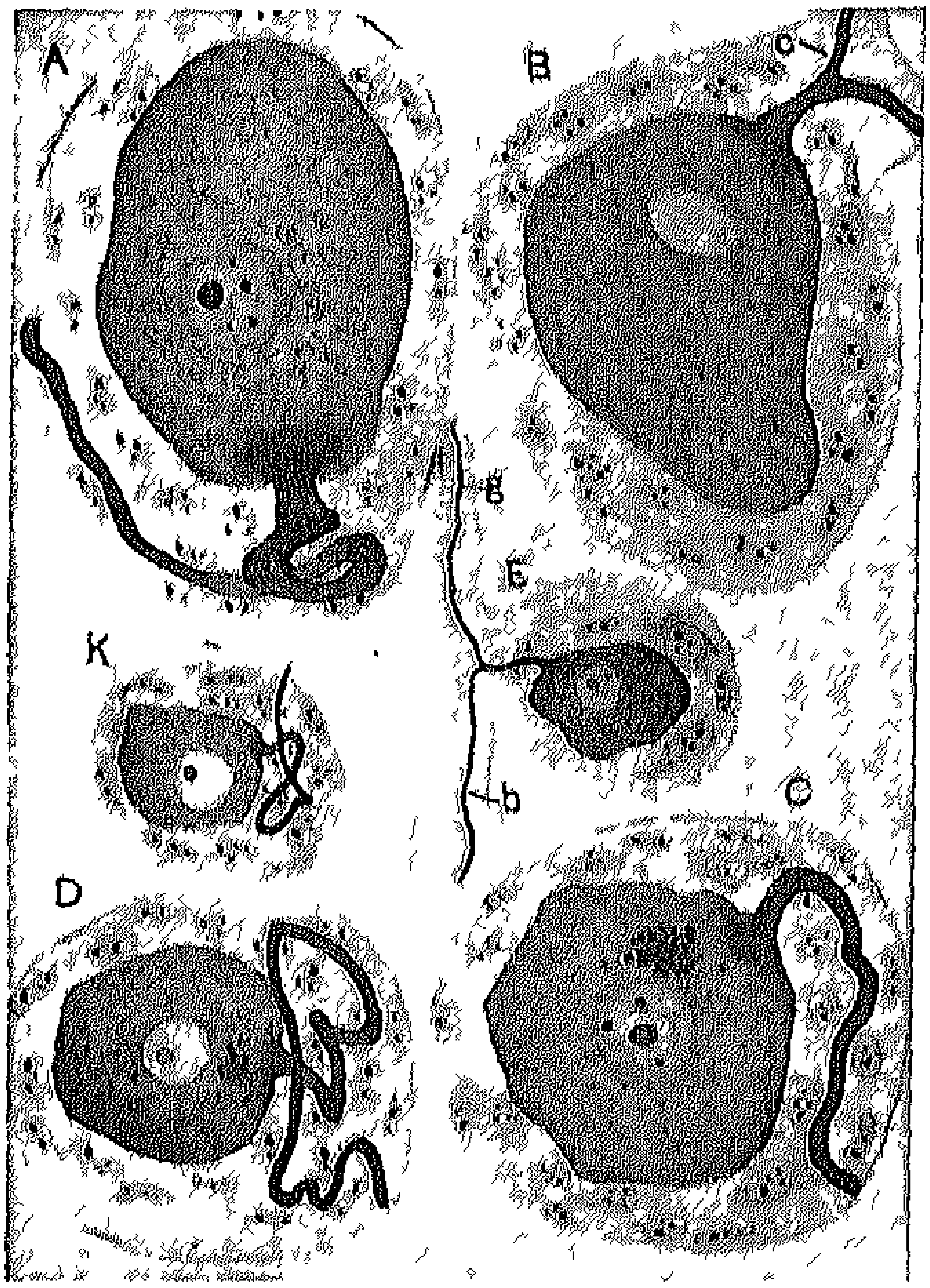


FIG. 78. Monopolar cells (sensory protoneurons) from diverse cerebrospinal ganglia. Normal, adult man. (A) Large cell with glomerulus from a cervical spinal ganglion. (B) Large cell without glomerulus from nodose ganglion of vagus (C, D, E and K) Large, medium-sized and small cells from Gasserian ganglion. In L and K notice marked difference in numbers of satellite cells determined by presence or absence of axonic glomerulus Cajal method (alcohol-ammonia) (Courtesy, Penfield: "Cytology and Cellular Pathology of the Nervous System," New York, Paul B Hoeber, Inc.)

vesicular nuclei with one or more deeply stained nucleoli. Some of the cells in the autonomic ganglia may have two nuclei. These cells, likewise, have a nucleated membranous capsule around them. Some of the dendrites of these ganglion cells branch and coil within the capsule *(intracapsular dendrites)*, while others pierce the capsule *(extracapsular dendrites)* to terminate at a distance from their parent cell.

Some of the autonomic cells (terminal ganglia of the intestinal wall) have no capsules.

NERVE ENDINGS

Nerve fibers terminate in relation to other nervous elements, and in relation to non-nervous tissues. This section will deal only with the latter.

Some nerve terminals receive stimuli and translate them into sensory impulses *(receptors)* while others terminate in relation to various organs, such as muscles and glands, to which they convey motor impulses that arouse these organs into a state of activity *(effectors)*. Nerve endings are thus classified as sensory or motor.

The function of the receptor organ is to translate various "environmental" stimuli into nerve impulses. For the most part, these stimuli reach the individual by way of the skin *(exteroceptive stimuli)* and they

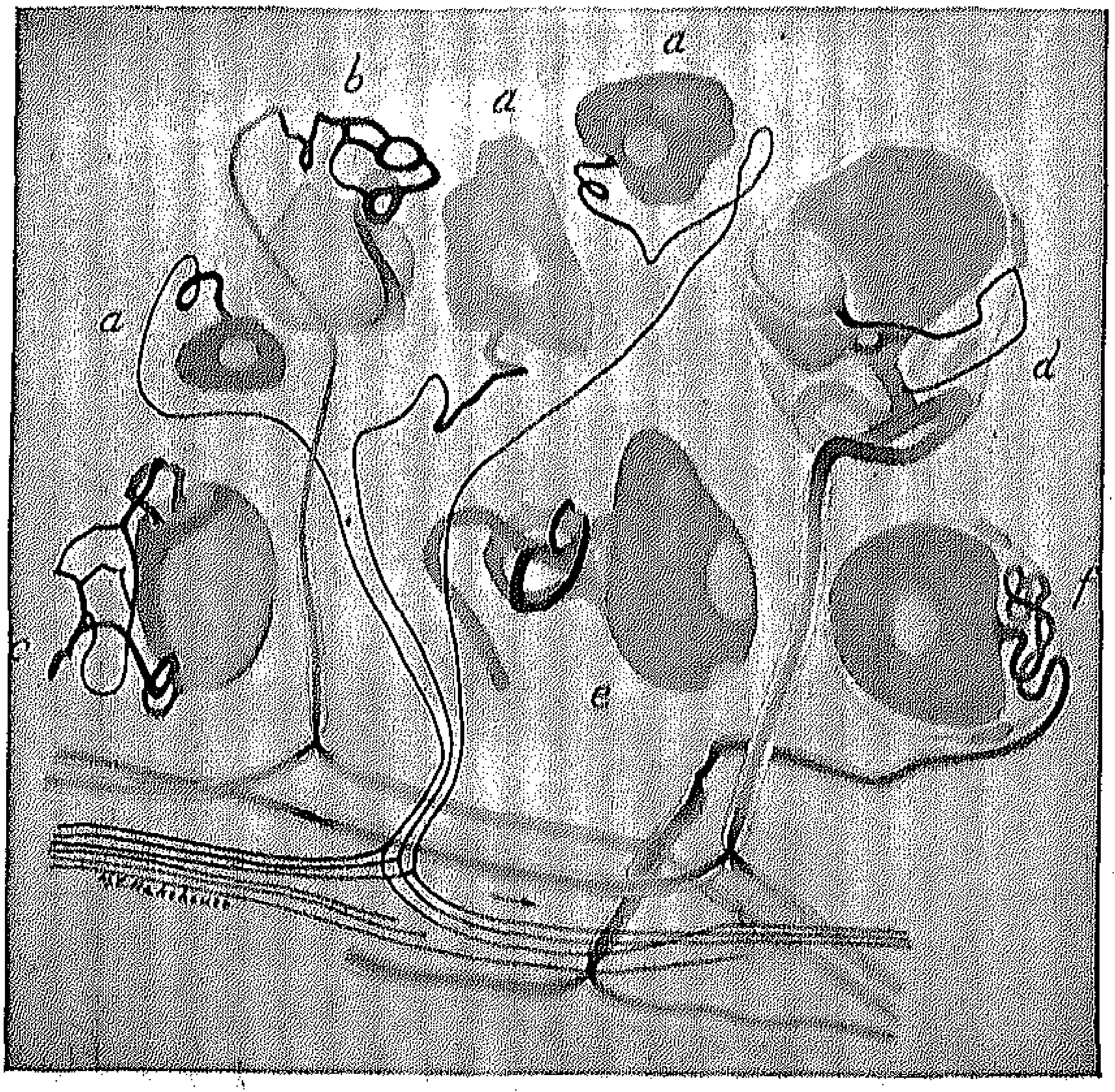


FIG. 79. Neurons from the spinal ganglion of a dog. *(a)* Small cells with unmyelinated axons. *(b, c, d, e,* and *f)* Large cells with myelinated axons. *(f)* Typical large spinal ganglion cell showing glomerulus and capsule. The arrow points toward the spinal cord. Pyridine-silver method. (From Ranson: "Anatomy of the Nervous System," 7th ed., Philadelphia, W. B. Saunders Co.)

include mechanical, chemical or forms of radiant stimuli, coming from outside the body. Included also in this group are stimuli from other tissues of the extremities or body wall. These are known as *proprioceptive stimuli.*

Each kind of stimulus has a specialized type of nerve ending which it is able to activate, all other endings being insensitive to that particular stimuli. Thus pain has one type of ending, touch has another, etc.

This general classification of nerve endings will not hold for the cranial nerve endings, which have highly elaborated extraceptors, even teleceptors being included. They are much more highly specialized and vary one from another; they will not be considered at this time, but will be described with the particular organs in which they are found.

SOMATIC AFFERENT NERVE ENDINGS. The sensory impulses which are conveyed by somatic afferent fibers are produced by: a. proprioceptive stimuli (stimuli from other tissues of the extremities

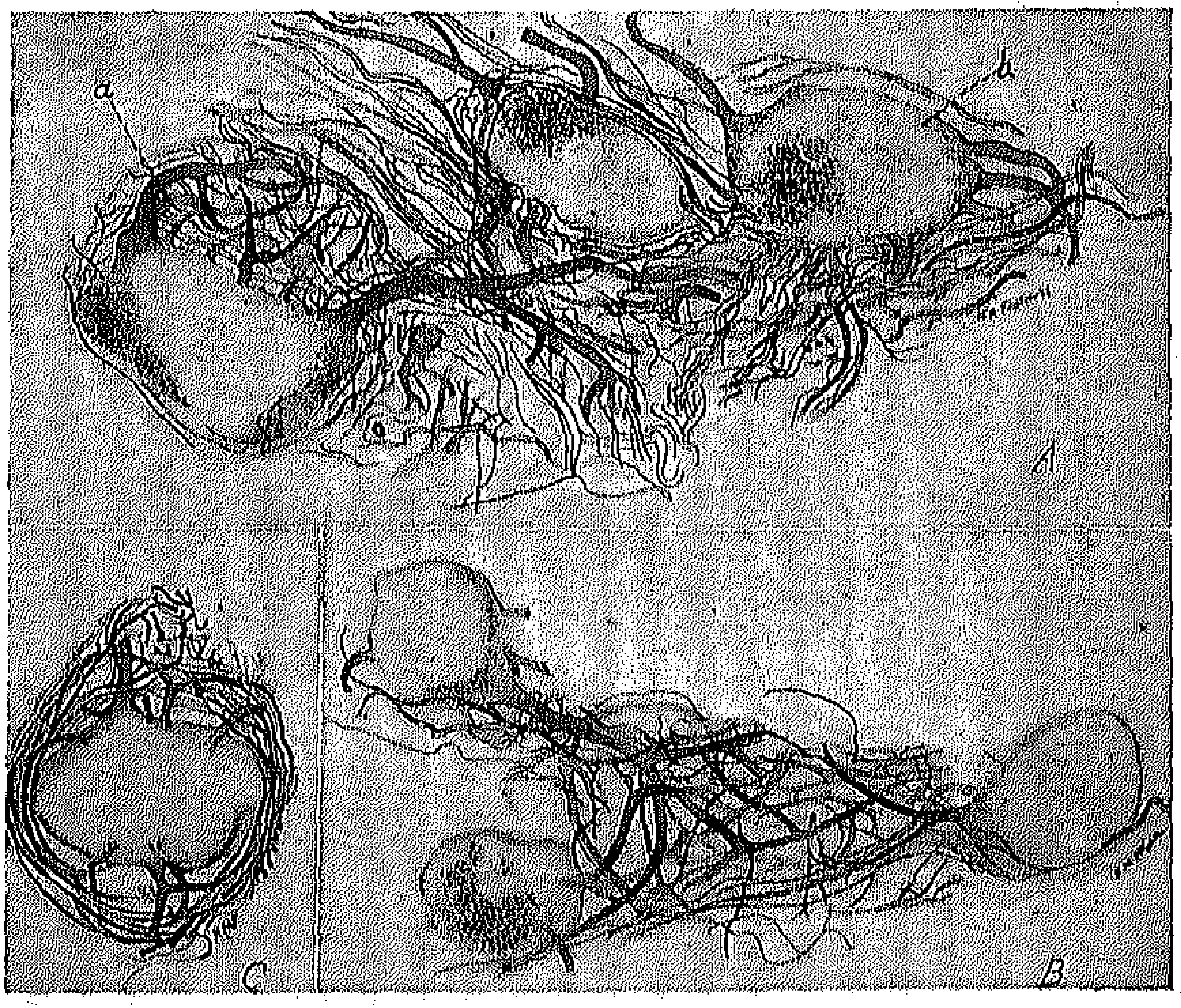


FIG. 80. Neurons from the human superior cervical sympathetic ganglion (pyridine-silver method). *(A)* Three nerve-cells and the intercellular plexus. *(a)* Unicellular glomerulus. *(b)* Neuron with extracapsular dendrites. *(B)* Tricellular glomerulus. *(C)* Neuron surrounded by subcapsular dendrites. (From Ranson: "Anatomy of the Nervous System," 7th ed., Philadelphia, W. B. Saunders Co.)

or body wall) or b. exteroceptive stimuli (those that come from outside the body). Both types of stimuli have as effector organs either *free nerve endings* or *encapsulated* structures known as *sensory end organs.*

PROPRIOCEPTIVE STIMULI. These stimuli affect three types of effector organs: (1) *Pacinian corpuscles* (encapsulated nerve endings); (2) *muscle spindles;* and (3) *neurotendinous end organs.* The fibers associated with these effector organs are myelinated.

(1) PACINIAN CORPUSCLES (CORPUSCLES OF VATER-PACINI). These structures occur in considerable numbers in the subcutaneous tissues of the hands and feet and in the tissues surrounding the nipple. They are also found in the tissue surrounding the tendons, ligaments and joints. In this last location they are thought to respond to changes in position and movement of the part. They also react to deep pressure as distinct from touch (light pressure). They are especially abundant in the mesenteries, in the vicinity of the blood vessels, and larger lymph glands. They occur also in the interstitial tissue of the pancreas and other organs.

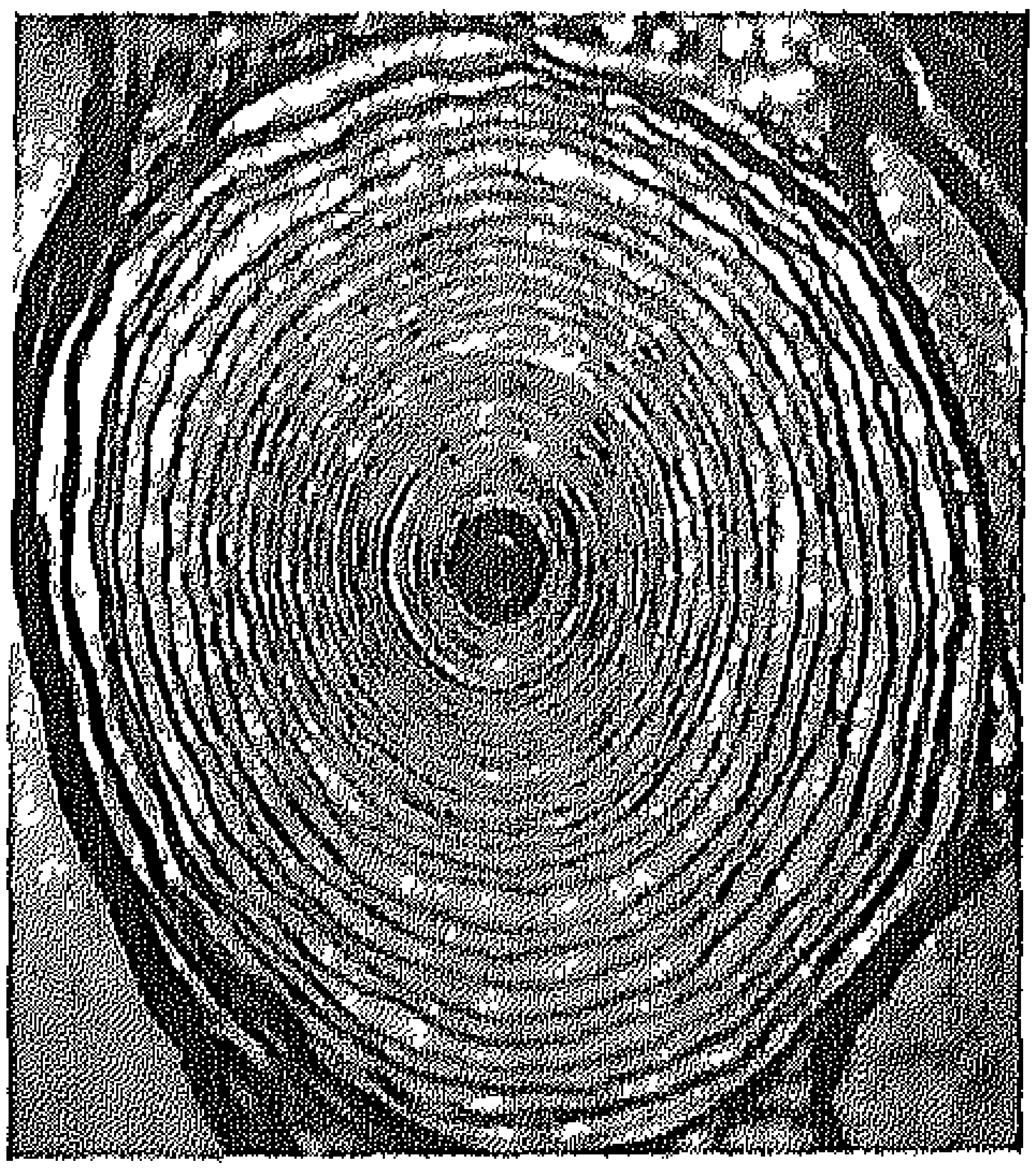


FIG. 81. Cross sections of a Pacinian corpuscle from the mesentery of the cat. Unretouched photomicrograph. (From a preparation by Heidenhain.) (Courtesy, Penfield: "Cytology and Cellular Pathology of the Nervous System," New York, Paul B. Hoeber, Inc.)

They are large, oval corpuscles having their associated nerve fiber embedded in a central core which is surrounded by a number of concentric connective tissue lamellae, which are lined by connective tissue cells so arranged that they simulate the appearance of an endothelium. The lamellae, which are formed by connective tissue fibers, are separated by spaces containing a lymphlike fluid. Besides one or more unmyelinated fibers, a single large fiber (myelinated) enters the capsule, its neurilemma sheath and sheath of Henle merging with the connective tissue of the lamellae. Its myelin sheath ends abruptly as it enters the core, the naked fiber traversing the core from one end to the other, ending in a knoblike expansion. Short side branches are given off by the nerve as it traverses the central core. A small artery enters with the nerve, its branches extending among the lamellae.

(2) MUSCLE SPINDLES. Sensory fibers end in striated muscles, in asso-

ciation with one or more modified muscle fibers enclosed within connective tissue, capsular sheaths. These structures are known as *muscle spindles* or *neuromuscular bundles*.

The muscle fibers of the spindles vary in number from one to several and are smaller than the ordinary fibers of striated muscle. They are rich in sarcoplasm. The muscle fibers are striated toward their ends, the striations becoming less distinct at the middle of the fiber where the sarcoplasm is most abundant and where the muscle nuclei are most numerous. The entire structure, which is spindle-shaped, or cylindrical, is enclosed within a capsule formed by a thickening of the connective tissue of the perimysium. The space within the capsule is filled with a perifibrillar fluid.

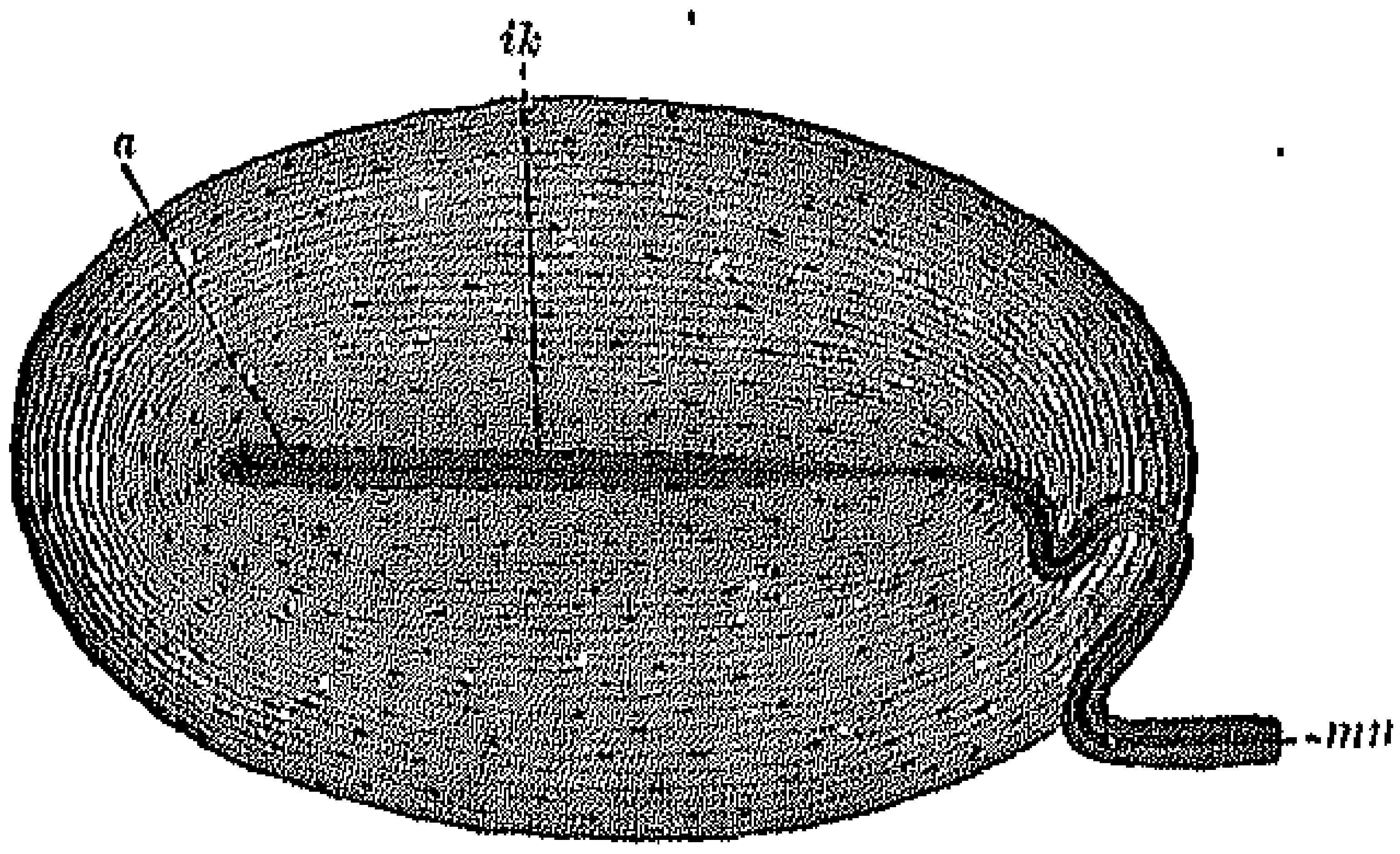


Fig. 82. Pacinian corpuscle showing concentric arrangement of lamellae about the core. *(a)* Axis cylinder. *(ik)* Inner core *(mn)* Medullated fiber entering core. (Sobotta.)

Muscle spindles are supplied by both sensory and motor nerves. The sensory nerve fibers, of which there are three or more, lose their investing sheaths as they enter the capsule, the sheaths of Henle merging with the capsular tissue. The myelin sheath disappears and the naked fiber breaks up into numerous, treelike branches which are closely applied to the surface of the sarcolemma *(epilemmal endings)*. These branches frequently wind around the muscle fibers in the form of rings or spirals.

(3) NEUROTENDINOUS END ORGANS (ORGANS OF GOLGI). These structures are found in relation to the musculotendinous junction. They consist of several tendon bundles which form a spindle-shaped structure enclosed by a thin capsule. One or more myelinated sensory fibers enter the end organ and break up into numerous branches which form complex networks on the tendon bundles. As usual, the myelin and sheaths of the nerve fiber are lost as it enters the capsule and only naked fibers are found within the substance of the end organ. These

end organs record changes of tension in the muscles and the tendon, resulting in change of position and movement.

EXTEROCEPTIVE STIMULI. These stimuli reach the body from the outside, therefore, the effector organs of this group are usually

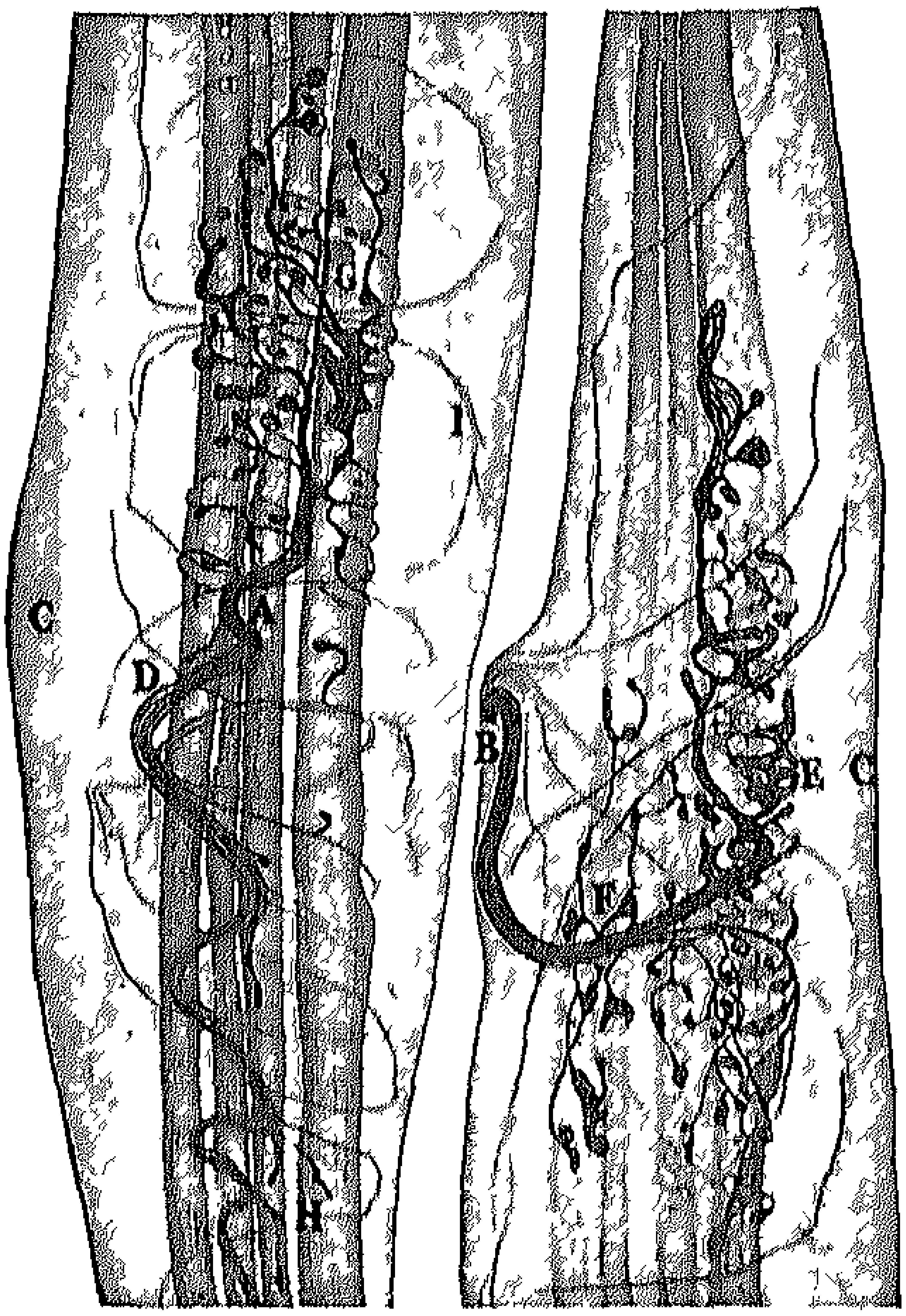


FIG. 89 Neuromuscular spindle of a human fetus of six months (A) Large ramifying fiber in shape of claws (G and B) Large hederiform termination (J. and C.) Connective tissue sheath (H) Motor fibers (I) Fine fibers (Tello). (Courtesy, Bremer Weatherford "Textbook of Histology," Philadelphia, The Blakiston Company.)

located in the skin. They include: (1) *free endings;* (2) *encapsulated nerve endings:* (a) *Meissner's corpuscles,* (b) *end bulb of Krause;* (3) *peritrichial endings* (around hair follicles); and (4) *tactile corpuscles of Merkle.*

(1) FREE NERVE ENDINGS. Sensory fibers may end freely, as in the epidermis of the skin. In the skin, as the nerve approaches the epi-

dermis, it loses its investing sheaths and separates into numerous threadlike branches, which pass between the epithelial cells for varying distances (they do not go beyond the cells of the stratum granulosum). The fibers end in relation to, but do not penetrate the substance of the cells. Many of the fibers end in small, knoblike enlargements which are in contact with the surfaces of the cells.

Free endings (pain endings), in which the terminal fibers of sensory nerves penetrate between the cells of an epithelium, are found in the cornea of the eye, in the oral epithelium and in mucous and serous membranes. They also occur in connective tissues, the nerve fibers branching and anastomosing to form complicated networks between the collagenous fibers of the tissue. Nerve endings of this type are especially abundant in the dermal and subdermal tissues of the skin. These fibers frequently terminate in beadlike swellings.

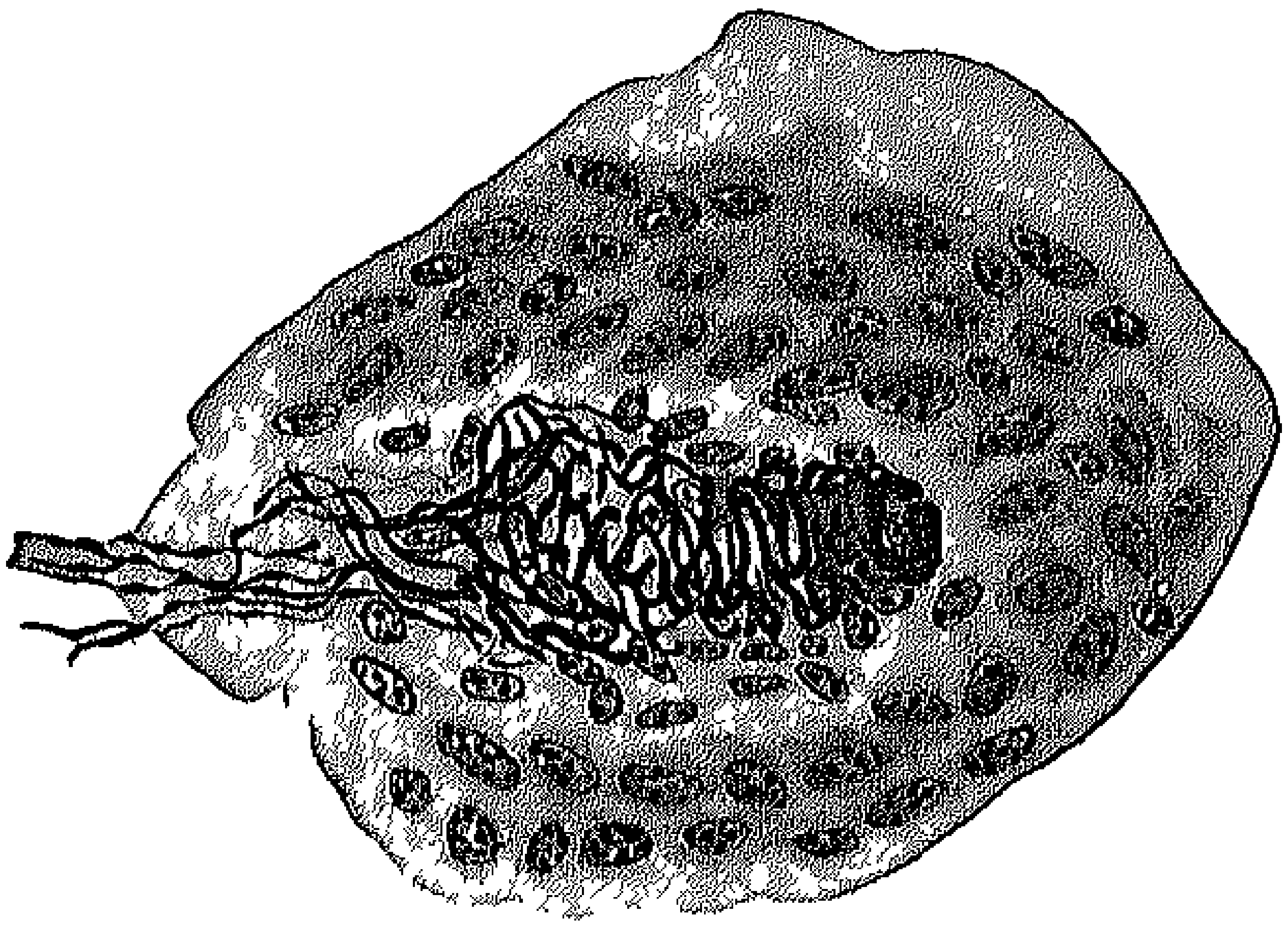


FIG. 84. Meissner's corpuscle in the skin of a finger of a six week's old child Golgi II Method (Rachmatullin). (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

(2) ENCAPSULATED END ORGANS OF THE EXTEROCEPTIVE GROUP INCLUDE: (a) *Meissner's tactile corpuscles* and (b) *end bulb of Krause.*

(a) *Meissner's Corpuscle.* The tactile corpuscles of Meissner are found most abundantly in the connective tissue papillae beneath the epidermis of the palm of the hand, the sole of the foot, and in the tips of the fingers and toes. They occur also in the forearm, lips, etc. They record the sensation of touch. In shape they are oval or cylindrical and are enclosed in a thin connective tissue capsule. They may be recognized by their transverse striations or markings, which are due to the horizontal arrangement of the cells which extend into the corpuscles from the capsule, and the sensory cells or *tactile plate.* The corpuscles receive one to four myelinated nerve fibers, which lose their investing sheaths, the connective tissue sheath of Henle merging with the tissue of the corpuscle. The naked axons enter the corpuscle and follow a spiral course between the tactile plates, their numerous branches ending between the plates in knoblike enlargements or networks. Unmyelinated fibers also are found in the corpuscle, but their significance is not known.

(b) *End Bulb of Krause.* These are the simplest type of encapsulated end organs. They are round, oval and sometimes elongated structures in which the nerves end in a number of branches that form interlacing, glomeruluslike coils within the lamellated capsule. They are found in the conjunctiva, the mucous membranes of the oral cavity, the synovial membranes of the joint cavities, and in the connective tissues in the various parts of the body. End bulbs, which are structurally similar to the end bulbs of Krause, but which are considerably larger and receive a greater number of nerve fibers, are found in the tissue of the glans penis and clitoris. These are known as *genital corpuscles.*

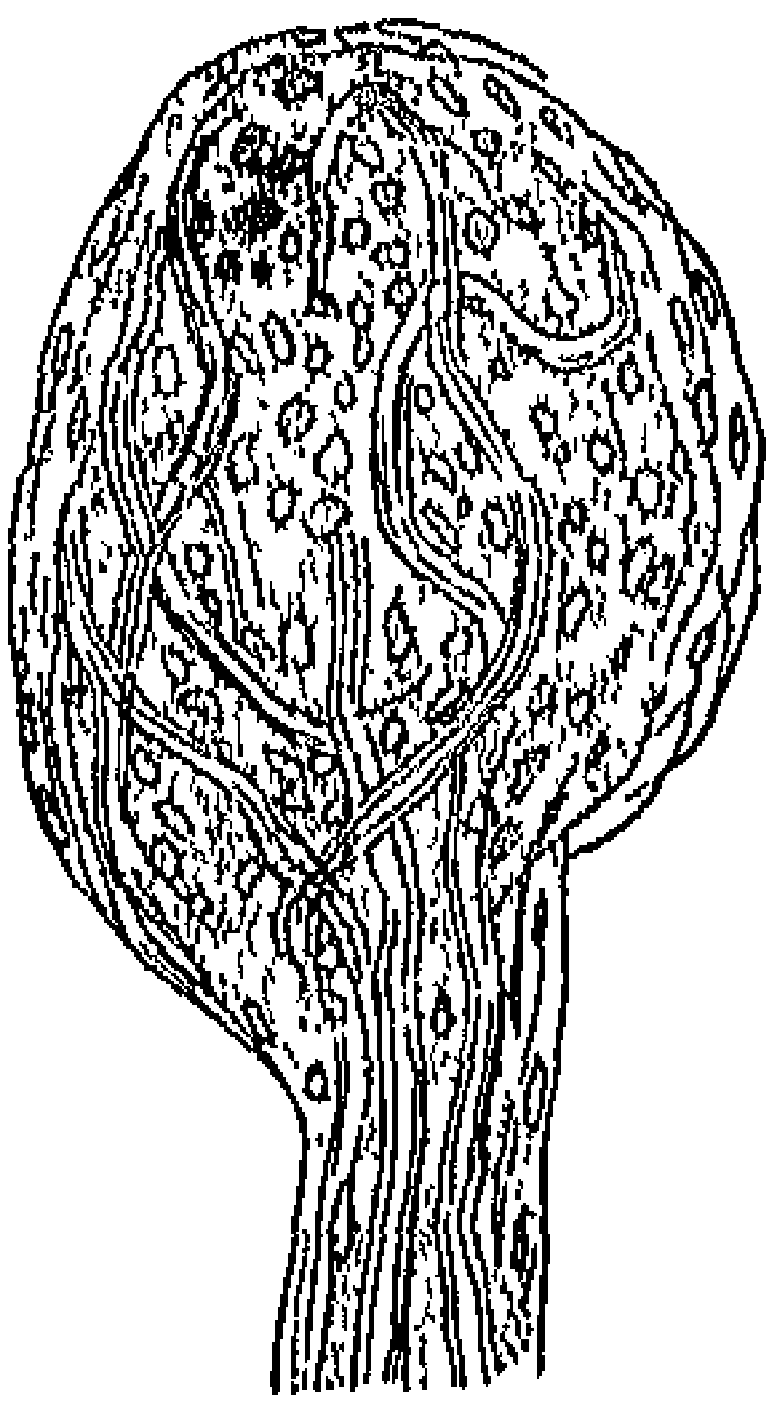


FIG. 85. End bulb of Krause from conjunctiva (human) Bielschowsky. (Courtesy, Gondinier: "The Anatomy of the Central Nervous System," Philadelphia, The Blakiston Company.)

(3) PERITRICHIAL ENDINGS. These are another form of the free ending. The fibers, as they approach the hair follicle, break up into numerous fine branches which encircle the follicle and end in relation to cells of the outer root sheath. These fibers receive tactile stimuli.

(4) TACTILE CORPUSCLE OF MERKEL. Nerve fibers ending in the deeper layers of the epidermis have peculiar expansions of the nerve terminal. This consists of a disc-shaped structure known as a *meniscus (tactile disc)* which lies in contact with modified epithelial cells. These structures are known as Merkel's tactile corpuscles.

SOMATIC EFFERENT NERVE ENDINGS. The motor fibers, which convey motor impulses to striated muscles, arise from cells located in motor nuclei of the brain and in the ventral horns of the spinal cord. The axons leave the central nervous system by way of the ventral roots *(motor roots)* of the spinal nerves. The fibers of these nerves enter the perimysium of the muscles where they divide into numerous smaller branches which pass to the individual muscle fibers. Thus one neuron may innervate several neurons and also one muscle fiber may receive nerve branches from more than one nerve fiber. As the nerve pierces the perimysium, the connective tissue sheath merges with the perimysium. The myelin sheath ends abruptly and the fibers continue to the individual muscle fibers. As the nerves pierce the sarcolemma of the muscle fiber, the neurilemma sheath fuses with it. The Schwann cells accompany the fibers which penetrate the sarcolemma; the nerve breaks up into several terminal fibers which ramify in the substance of a mass of differentiated sarcoplasm, known as the *sole plate,* about which a number of muscle nuclei are gathered. The entire structure is known as a *motor end plate.* Since these nerve endings extend beneath the sarcolemma they are called *hypolemmal endings.*

VISCERAL EFFERENT NERVE ENDINGS. The nerve fibers which carry motor impulses to the smooth muscles, the secretory cells of glands, and to the muscles of the heart, are from the autonomic system. They are unmyelinated fibers. These fibers divide into numerous branches, to form plexuses around bundles of smooth muscle.

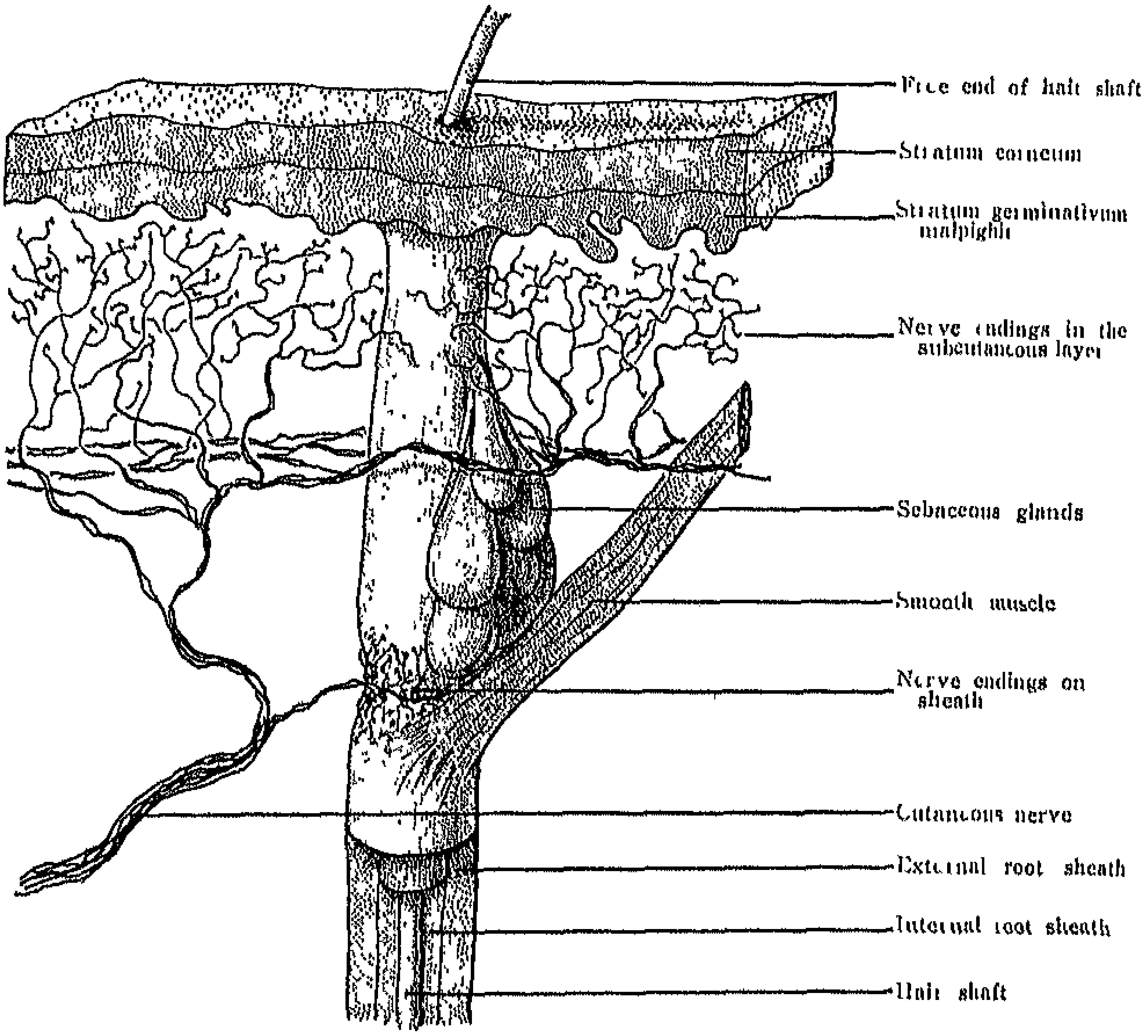
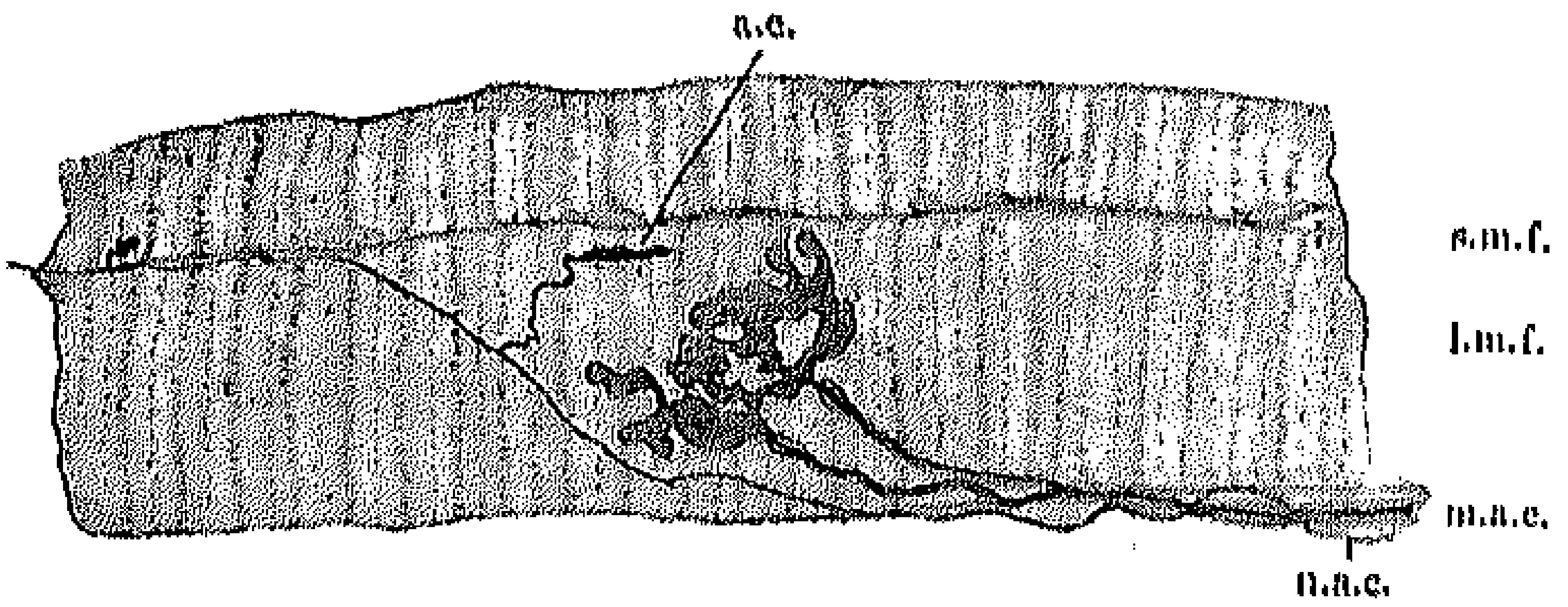


FIG. 86. Peritrichial nerve endings. A form of free nerve endings about hair follicles.



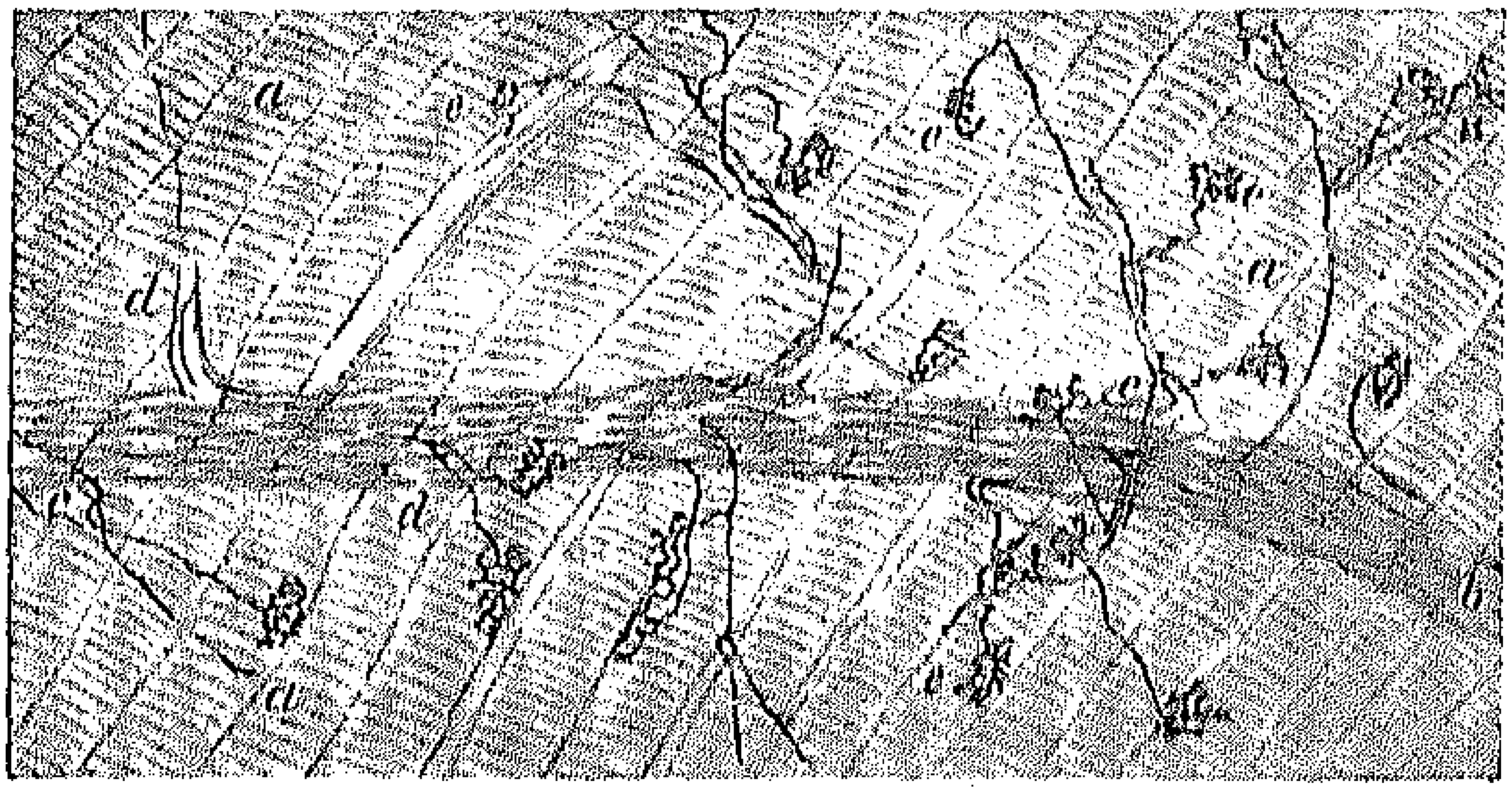


FIG. 87. *(Top)* Longitudinal section of striated muscle showing motor nerve endings. (m.a.c.) Medullated nerve fiber. (n.a.c.) Non-medullated nerve fiber which contributed an accessory epilemmal ending (a.e.) to the large muscle fiber (l.m.f.) and another similar ending to the smaller muscle fiber (s.m.f.). (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

FIG. 88. *(Bottom)* Motor terminations on striated muscle fiber (lizard). *(a)* Muscular fibers. *(b)* A nerve trunk which splits up into small branches, *c*, containing a few medullated fibers, *d*. The medullated fibers, *d*, end in motorial end plates, *e*. (Courtesy, Gordinier: "The Anatomy of the Central Nervous System," Philadelphia, The Blakiston Company.)

Fine nerve fibers go from these plexuses to end in terminal expansions, applied to the individual smooth muscle fibers. Nerve fibers end in relation to heart muscle in a manner similar to their endings in smooth muscle, their terminal fibers lying beneath the sarcolemma. The nerve fibers which supply motor impulses to glandular structures, first form a plexus beneath the basement membrane. Fibers from this plexus terminate on the gland cells, and have been described as penetrating the cell to end intracellularly.

NEUROGLIA

The interstitial or supportive tissue of the central nervous system, except for the fibrous connective tissue forming the coverings of the brain and cord (meninges), and that accompanying blood vessels, is composed of a specialized type of nervous connective tissue called *neuroglia.* It is composed of cells and their processes. These cells may be classified as: *astrocytes (astroglia); oligodendroglia; microglia (mesoglia);* and *ependymal cells.* Certain cells which act in a similar capacity in relation to the peripheral nerves, and which should, therefore, be included are: the *mantle cells,* which serve to encapsulate the ganglion cells; and the cells of the neurilemma sheath. Except for the microglia cells, all of the rest of the cells are derived from ectoderm; microglia are said to be of mesodermal origin, although this has been denied, and are carried in by the blood vessels.

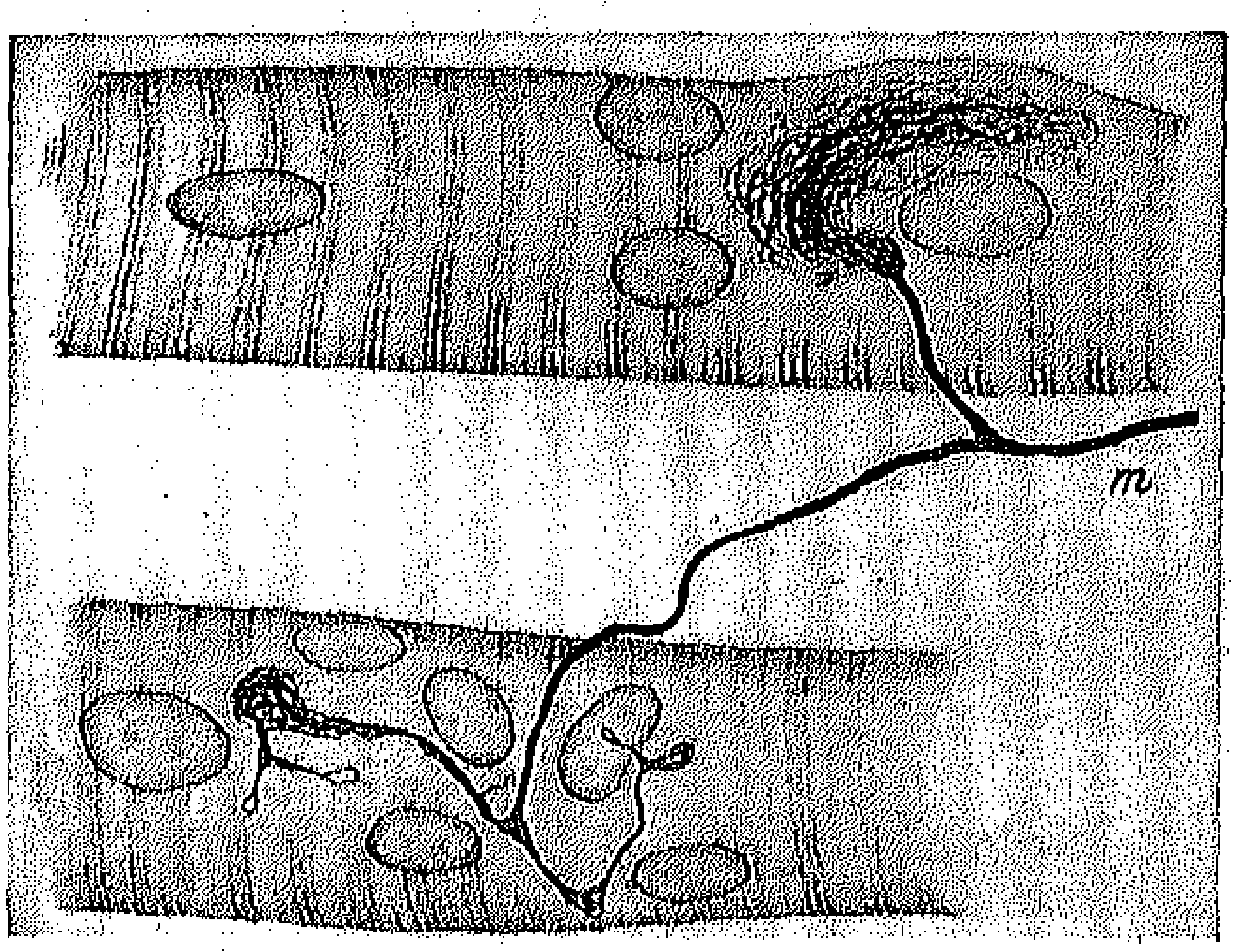
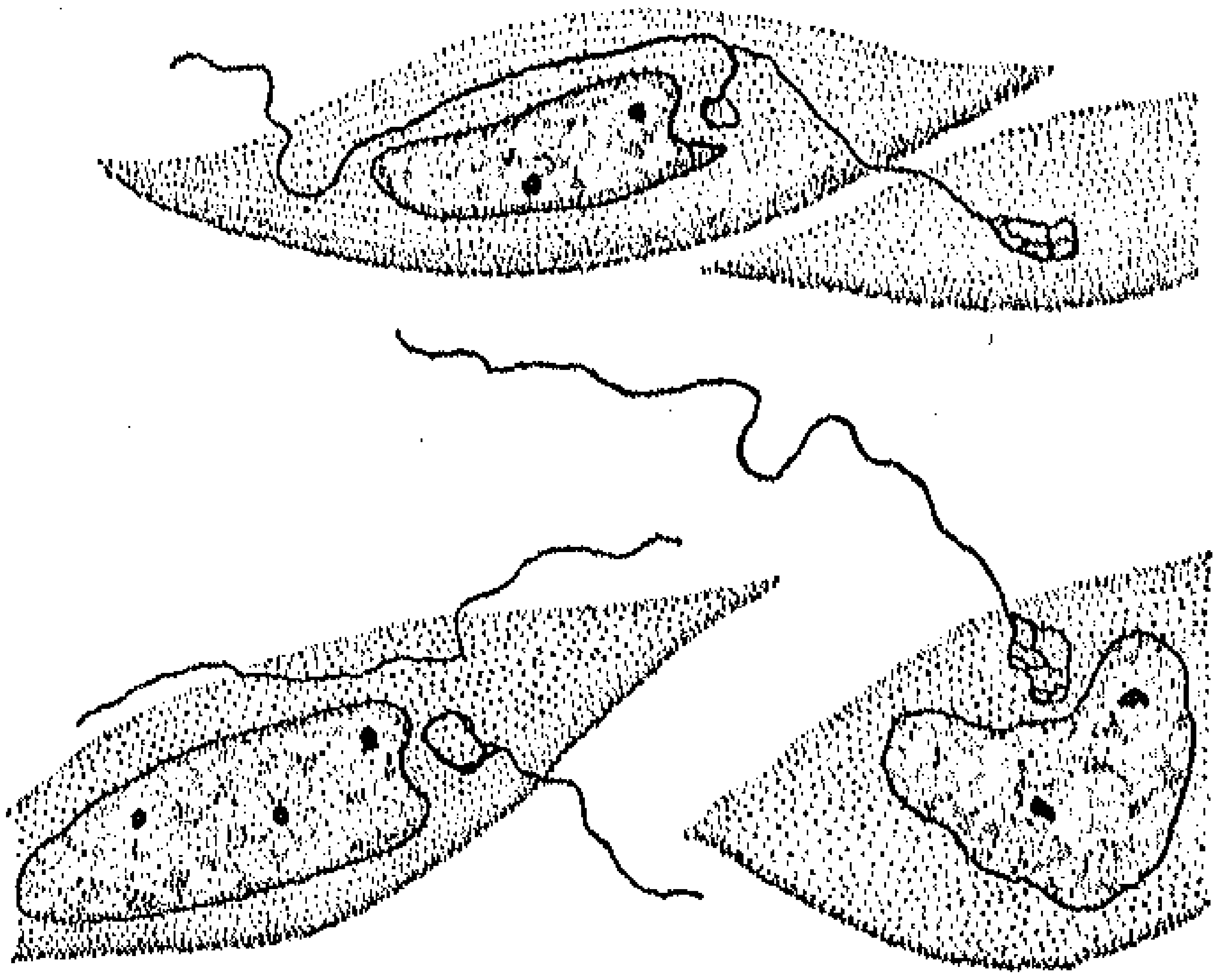


FIG. 89. Two different types of motor endings on the same nerve fibers from the tongue (mouse). The motor ending on the upper muscle fiber shows a periterminal network. The terminals on the lower muscle fiber end in loops. (Courtesy, Penfield: "Cytology and Cellular Pathology of the Nervous System," New York, Paul B. Hoeber, Inc.)

ASTROCYTES (ASTROGLIA). Astrocytes are neuroglia cells which have small stellate-shaped protoplasmic bodies, and relatively large, round, or oval nuclei containing only a small amount of chromatin. They have many processes which radiate out from the cell body in all directions and branch rather profusely. They make up the greater part of the supportive elements of the gray matter of the brain and cord. They are multipolar cells. Astrocytes are of two kinds: 1. *fibrous astrocytes;* and 2. *protoplasmic astrocytes.*

FIBROUS ASTROCYTES. These cells occur in both the white and gray matter of the central nervous system, but they are much more abundant in the white matter. The fibrous astrocytes are characterized by delicate, unbranched fibers (neuroglia fibers) extending through both the body and protoplasmic processes of the cell. Their processes are longer and straighter than the processes of the protoplasmic astrocyte.



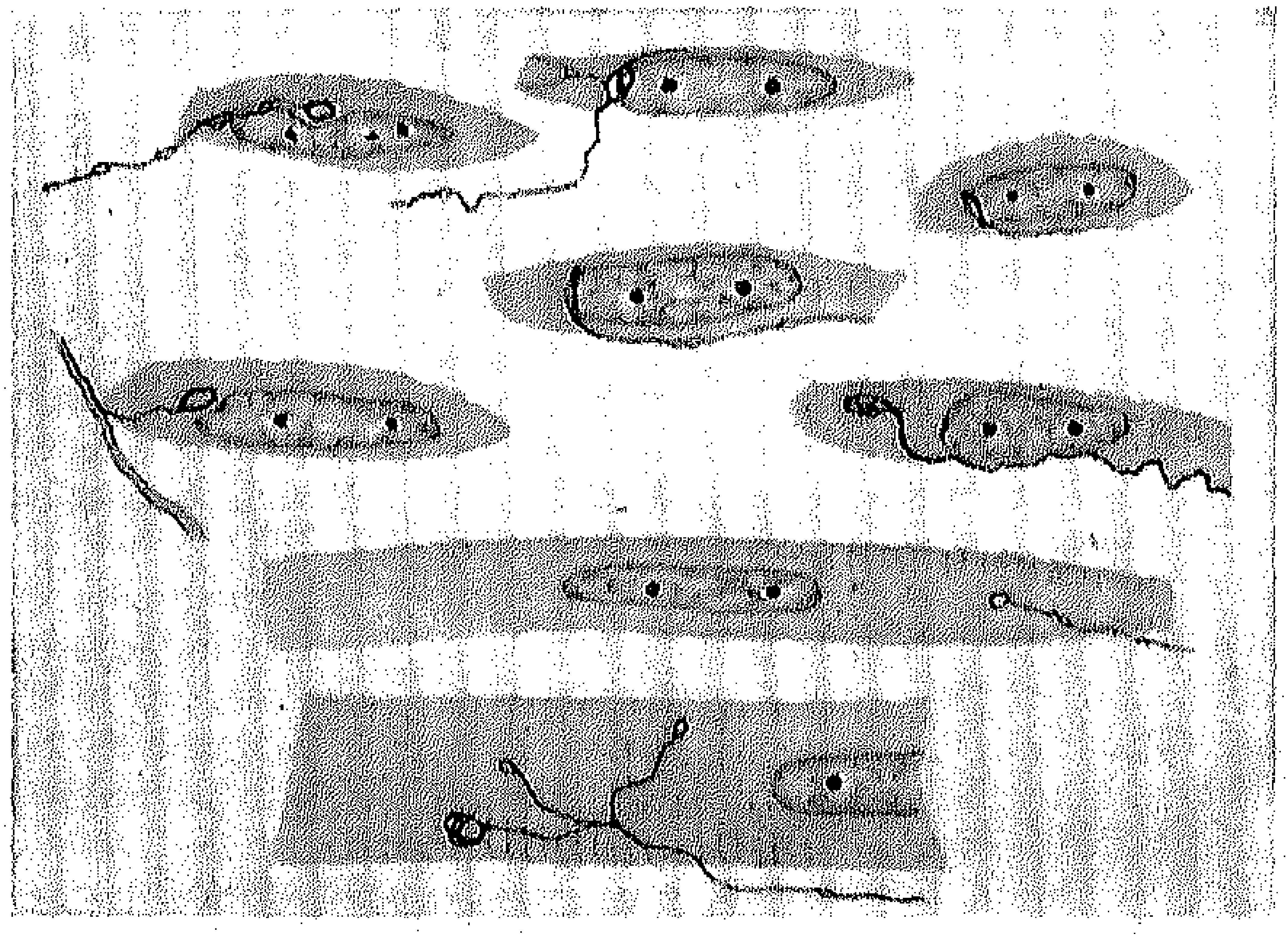


Fig. 90. Nerve endings on smooth muscle cells of corpus ciliare of the human eye penetrating into the cells.

Fig. 91. Nerve endings in cardiac muscle (tortoise). (After Boeke, 1924.) (Courtesy, Penfield: "Cytology and Cellular Pathology of the Nervous System," New York, Paul B Hoeber, Inc.)

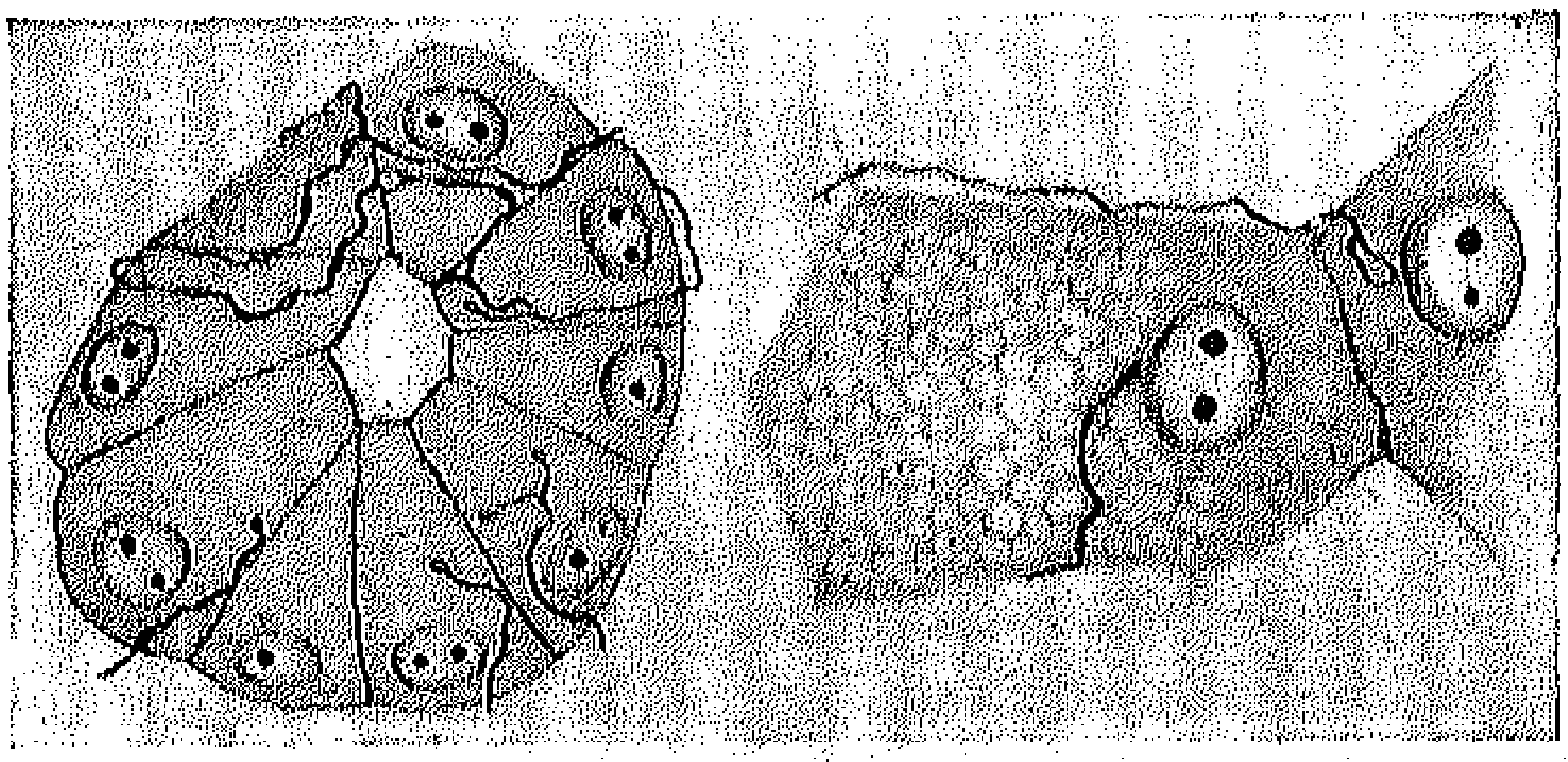


FIG. 92. Nerve endings in the alveoli of the lacrimal gland *(left)* and inside two cells *(right)*. Bielschowsky method. (Courtesy, Penfield: "Cytology and Cellular Pathology of the Nervous System," New York, Paul B. Hoeber, Inc.)

However, these processes like those of the protoplasmic astrocyte, also terminate in knoblike expansions called *perivascular feet.*

PROTOPLASMIC ASTROCYTES. These cells are found principally in the gray matter of the central nervous system. They are distinguished from the fibrous type by their thicker, branched processes and the absence of fibers.

Astrocytes appear in relation to blood vessels, to which they are attached by one or more relatively thick processes, which end in expansions called *perivascular feet (foot plate).* Astrocytes are also attached to the pia, where together with the other neuroglia cells they form the *pia-glial membrane.* This membrane covers the brain, spinal cord, and forms sheaths which enclose and accompany the blood vessels as they penetrate the substance of the brain and spinal cord.

OLIGODENDROGLIA. These cells are not as large as astrocytes. They are characterized by having small, round nuclei in which the chromatin is in the form of fine granules and by relatively few, slender processes which do not branch freely. There are no perivascular feet at the ends of the processes, but in their relationship to blood vessels, the cell body rests against the surface of the small vessels. They occur in both the gray and white matter of the brain and cord. In the gray matter they are closely associated with the nerve cells and blood vessels, and are known as *satellite cells.* In the white matter they are abundant, and are arranged in rows between the myelinated fibers, where they appear to take the place of the neurilemma cells. Like the neurilemma cells they are thought to regulate the formation of myelin and they may participate in neuronophagia.

MICROGLIA (MESOGLIA). Microglia are small multipolar cells (some few are bipolar) in which the irregularly oval, or bent, nuclei are considerably darker than the nuclei of the astrocytes and oligodendroglia. The scanty cytoplasm sends out long, slender, branched processes on which are a number of irregular, spinelike enlargements. However, they have no perivascular feet on their processes. Microglia cells occur in both the white and gray matter of the central nervous system. They are frequently found in the region of blood vessels, but are not attached to their wall by perivascular feet. These cells may arise in relation to the pia and enter the brain along with the blood vessels. They are the scavenger cells of the central nervous system, the function of which under normal conditions would be restricted to the removal of the breakdown products of the metabolism of nervous tissue. However, they reach the height of their functional capacity under pathological conditions in the nervous system. They then become actively ameboid and phagocytic. They swell and become known as *gitter cells* or *compound granular corpuscles.*

Identification of neuroglia cells of the central nervous system in Nissl stained preparations is dependent on recognition of their nuclei, which are quite typical. They can be distinguished from nerve cells by the absence of nucleoli. The nuclei of astrocytes are round or oval in shape and have relatively little chromatin material, which occurs in granular form. Because of the scant amount of chromatin material the nuclei stain lightly. In size these nuclei are about the same as the nuclei of small neurons. The nuclei of oligodendria are smaller than

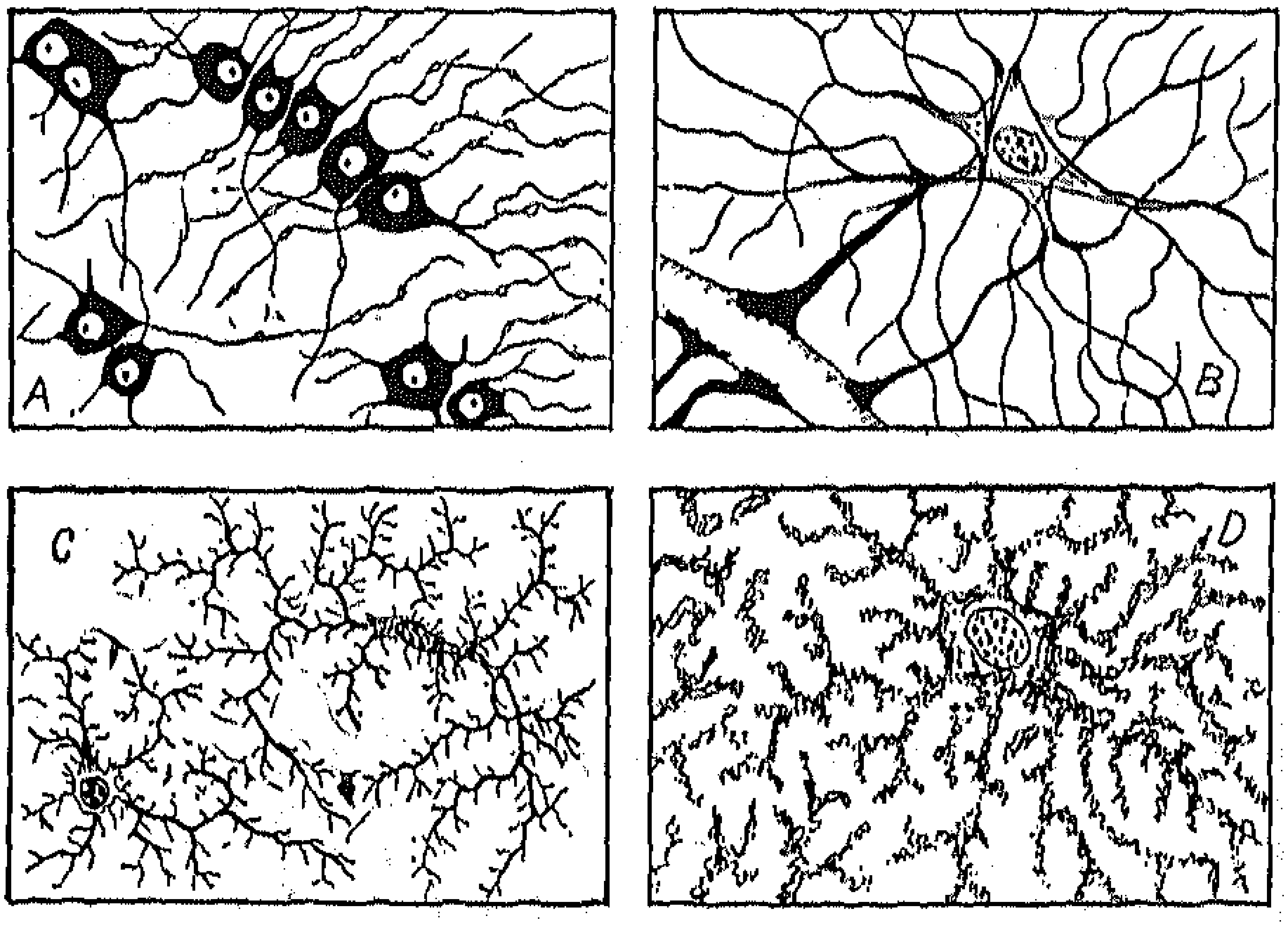


FIG. 99. Diagrammatic representation of interstitial cells of the central nervous system. (A) Oligodendroglia. (B) Fibrous astrocytes. (C) Microglia. (D) Protoplasmic astrocytes. (From Krieg, after Hortega, from Grinker's "Neurology," 1st ed., courtesy, Charles C Thomas, Springfield, Ill.)

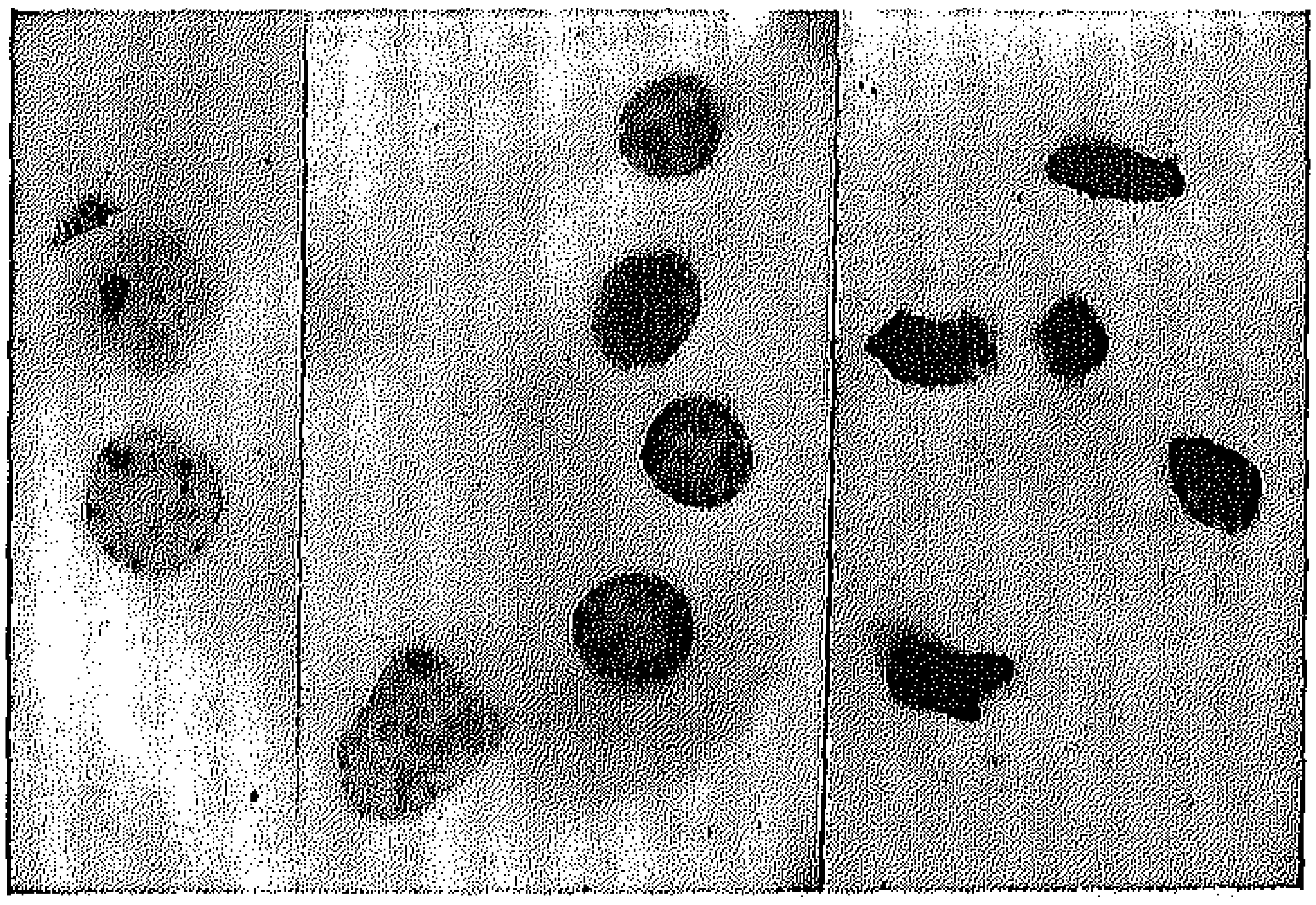


FIG. 94. Nuclei of astrocytes *(left)*, oligodendroglia *(center)*, and microglia *(right)*. Stained with cresyl violet. Photograph by Weil. (From Ranson: "Anatomy of the Nervous System," 7th ed., Philadelphia, W. B. Saunders Co.)

those of the astrocytes and they are more darkly stained. The smallest nuclei belong to the microglia. Their shape is variable, some are round, others are quite elongated and may appear straight or bent in a C-shape. They are more deeply stained than the nuclei of either of the preceding two cells.

EPENDYMAL CELLS. These are simple columnar cells with elongated nuclei. A long slender process extends from the base of the cell rather deeply into the underlying nervous tissue. A few cilia project from the free surface of the cell (in the embryo, the cilia are more numerous, but only a few remain in the adult). These cells line the ventricles of the brain and the central canal of the spinal cord.

THE MENINGES

The meninges are the connective tissue coverings of the brain and spinal cord. They consist of three separate membranes, the outermost being the *dura mater,* the middle the *arachnoid,* and the inner the *pia mater.*

The outer membrane or dura is formed of dense fibrous tissue. In the cranium, where it is fused with the periosteum, it consists of two layers. The outer or periosteum is a vascular, connective tissue layer. The inner portion or dura proper is a less vascular, more compact and less cellular layer of dense connective tissue covered by a layer of flattened mesenchymal epithelial cells. At certain points, the inner layer forms free folds which extend into the cranial cavity, where it forms partitions or septa. These folds are: the *falx cerebri* which extends into the median fissure that separates the cerebral hemispheres, the *falx cerebelli* that is a similar fold located in the posterior fossa. It likewise projects forward in the midline. The *tentorium cerebelli* covers the posterior cranial fossa, and extends between the occipital lobes of the cerebrum and the cerebellum.

The arachnoid or middle layer is separated from the dura by the subdural space. It is a thin, avascular, weblike membrane composed of interwoven bundles of collagenous fibers and elastic fibers. While the arachnoid itself is avascular, blood vessels pass through it to enter the brain. As the blood vessels traverse the arachnoid they are enclosed by this membrane and it forms an investing sheath which accompanies the vessels as they penetrate the substance of the brain. In this location the arachnoid forms the adventitial layer of the wall of the vessels, only the capillaries being devoid of this layer. The surface of the arachnoid toward the dura is smooth, but from its inner surface numerous fibrous strands extend across the subarachnoid space to the pia. The subarachnoid space is also lined by mesenchymal epithelium.

The pia mater is the inner membrane. It is a delicate, vascular layer of connective tissue which closely invests the brain and spinal cord. It contains the blood vessels which go to the brain and it forms investments for the vessels when they enter the brain tissue, and in this

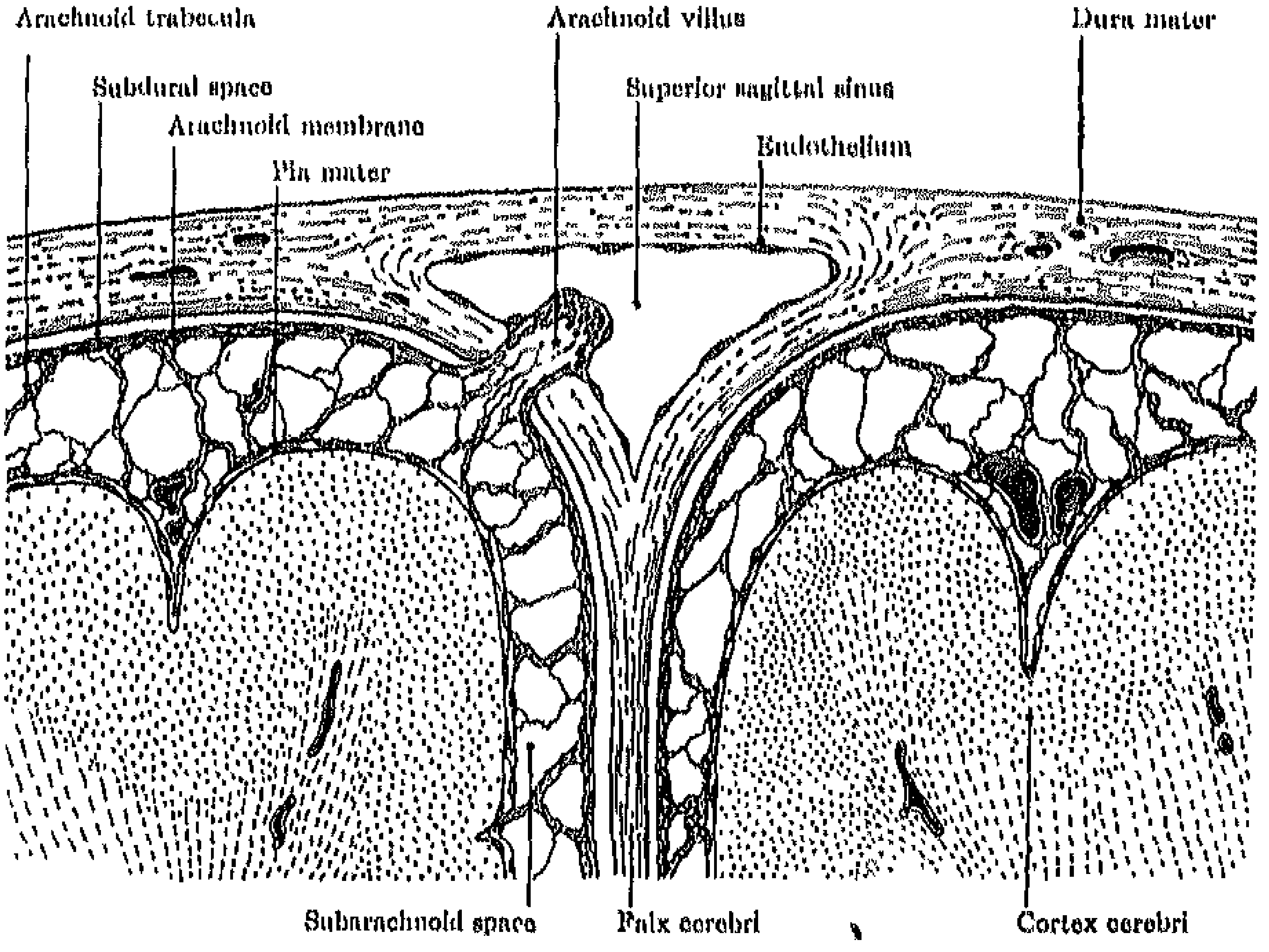


FIG. 95. Diagram representing a coronal section through superior sagittal sinus to show relation of meninges. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

relationship forms the outer wall of the so-called vascular space. In the pia covering the spinal cord, the collagenous fibers are roughly arranged in an inner circular and an outer longitudinal layer.

Both the pia and the dura are well supplied with nerves. The nerves to the pia are derived from the autonomic system and are distributed to the walls of blood vessels. Besides the autonomic nerves to the blood vessels, the dura also receives many sensory fibers which terminate in the connective tissue in enlarged or swollen endings or in end organs similar in appearance to Meissner's corpuscles.

SUMMARY

DEFINITION: Nervous tissues are highly specialized tissue for the reception, transmission and coördination of nervous impulses.

Nervous System.

1. Brain
2. Spinal cord
3. Peripheral nerves
4. Ganglion
5. End sense organs

Nervous Tissue.

Composition: 1. Nerve cells or neurons
2. Nerve fibers
3. Neuroglia or the supporting tissue
4. End sense organs

NERVE CELL: Consists of the cell body and its processes (axons and dendrites).

The cell body and the dendrite are very much alike structurally. Both contain Nissl substance, the neuroplasm is fluid and will escape if the cell membrane is ruptured. If the axon is severed, the cell body and dendrite do not die; they are not dependent on the presence of the axon.

CHARACTERISTICS OF A NERVE CELL

	Characteristic Features	*Shape*	*Size*	*Location*	*Cytoplasmic Constituents*
1. Nerve Cell	Processes: axons and dendrites	Variable Round Spindle Stellate	Variable (4-180 microns)	Gray matter of brain and spinal cord; ganglia of cranial and spinal nerves; ganglia of autonomic system	Granules (Nissl substance) Neurofibrillae Fat droplets Pigment granules Mitochondria Golgi apparatus
a. Nucleus	Well-defined nucleoli	Round or oval	Large	In or near center of cell	————

The axon, on the other hand, contains no Nissl substance. The neuroplasm is less fluid than that of the cell body and dendrites so that even if the membranes enclosing the axon are damaged, the neuroplasm does not escape. The axon cannot live if it is cut off from the cell body.

To fully appreciate the study of specially stained neurological material, it is essential to have some understanding of the selective action of some of the more commonly used stains. For detailed information the student will have to consult the more comprehensive books of techniques. For a brief survey of the subject the tabular summary on page 172 should prove helpful.

Name	Derivation	Size	Shape	Nuclei			Cytoplasm	Phagocytic
				Size	Shape	Chromatin		
Astrocytes Fibrous Protoplasmic	Ectoderm	Largest of glia cells	Variable but usually stellate Have branching processes that end in expansions by which they are attached to blood vessels and the pia mater	Relatively large	Round or Oval	Small amount	Fibrous type has many fibers Protoplasmic type has no fibers Mitochondria Pigment granules Golgi apparatus	No
Oligodendroglia	Ectoderm	Smaller than astrocytes	Oval cells with delicate, short, branched processes that give them a thorny appearance	Small	Round	More than in astrocytes Chromatin in form of small granules	No fibers	No
Microglia	Mesoderm	Smallest of glia cells	Oval with long slender branched processes	Smaller than oligodendroglia	Round	Much chromatin Nuclei stain deeply	Cytoplasm granular	Very

NEUROLOGICAL STAINS

Stain	*Structure Stained*	*Color*	*Value*	*Technique*
Osmic	Myelin sheaths	Black	Used for peripheral nerves Study of myelination of fibers—location and extent of myelinated fiber tracts	Fixation in osmic acid
Weigert or Pal-Weigert Method (also Weil's)	Myelin sheaths Everything else colorless	Blue	Used for central nervous system Study of myelination of fibers during development Extent of myelinated fiber tracts Study of degeneration of fiber tracts (remain colorless)	Fixation in Müller's fluid contains potassium bichromate) Myelin sheaths now stain with haematoxylin
Marchi Method	For degeneration of myelin sheaths	Normal myelinated fibers—light yellow Altered myelin (in droplet form) in degenerating fiber—black	Study of extent of degeneration of nerve fiber	Fixation in Muller's Stained with osmic acid
Silver Stains *Bodian* *Cajal* *Davenport* *Pyridine-silver technique*	Nerve cells and their processes—*particularly* the neurofibrils Myelin sheaths not stained	Yellow, brown or black	Used for central nervous system *and peripheral nerves* Study of nerve cells and extent and course of the processes	Treated with silver followed by *pyrogallic acid or hy*droquinon—reduces silver
Golgi Method	Nerve cells and their processes Neuroglia	Yellow, brown and black	For shape and extent of nerve cell and its processes For study of neuroglia	Silver impregnation
Basic Stains Toluidine blue Cresyl violet Nissl's methylene blue	Nissl bodies Nuclei	Blue to violet	To show distribution and character of Nissl bodies For study of nuclei	Formalin fixed material Stained with one of basic stains listed

11

The Vascular System

The vascular system consists of a series of vessels which contain the two principal fluids of the body, the blood and lymph. The vessels containing the blood, and through which it flows, constitutes the *blood vascular system;* those which contain the lymph *(lymphatics)* form the *lymph vascular system.* The blood vascular system forms a "closed system" while the lymphatic is usually considered to be an "open" system of tubes.

THE BLOOD VASCULAR SYSTEM

The blood vascular system consists of the *heart,* a large muscular organ which propels blood through vessels, and a series of several kinds of vessels that carry the blood from the heart throughout the body and back again to the heart. The change in structure from one kind of vessel to another is not abrupt, but gradual. These vessels in order are: 1. *Elastic arteries* (aorta, pulmonary, innominate, subclavian and the beginnings of the common carotid arteries); 2. *Muscular arteries;* 3. *Arterioles;* 4. *Capillaries;* 5. *Venules;* 6. *Veins.* The arteries and arterioles carry blood from the heart; the veins and venules return blood to the heart. The capillaries are extremely small, thin-walled vessels that connect the arterial side with the venous side of the system In some places in the body, the capillaries are replaced by sinusoids which, while having a few characteristics in common with capillaries, differ from them in several important aspects.

Throughout its entire extent, the vascular system (the heart and vessels) is lined by a continuous, unbroken layer of endothelial cells arranged as a simple epithelial layer. Because of this the vascular system is considered to form a *closed system.*

ARTERIES

ELASTIC ARTERIES. The elastic arteries include those arteries which arise from the heart and their branches. Because of their close proximity to the heart, these vessels receive the full force of the blood as it is expelled from the ventricles. In order to withstand the terrific pressure to which they are subjected, certain modifications have occurred in the structure of the walls of these vessels. These modifications consist of a marked increase in elastic tissue accompanied by a proportional decrease in the amount of muscular tissue. Moreover, in these vessels the various fibers take a spirally directed course around the vessel walls.

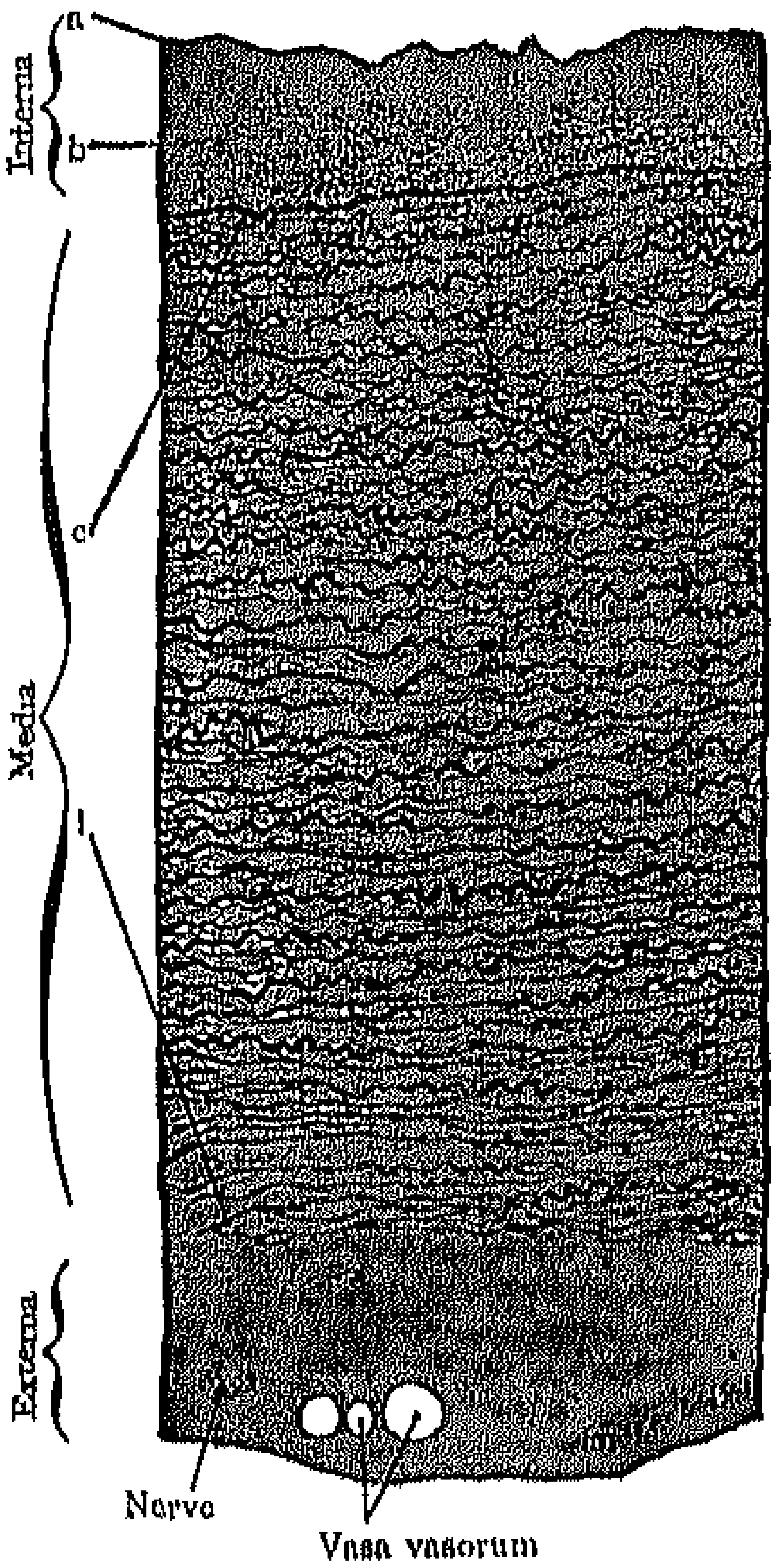


FIG. 96. From a transverse section of the human thoracic aorta, stained with resorcin-fuchsin. 80 ×. (a) Endothelium. (b) Subendothelial fibrous tissue. (c, d) Elastic membranes of the media. (Courtesy, Bremer Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

The great increase in the elastic tissue allows the vessels to expand when the blood is forced in by ventricular contraction. This force is transformed into pressure (by the elasticity of the arterial wall) that is released and becomes effective in forcing the blood onward during the period when the ventricles are relaxed (diastole). In *this way a rhythmically continuous, instead of an intermittent, pressure is maintained.*

In these vessels the *intima* consists of an inner layer of endothelial cells, an intermediate layer of connective tissue, and an outer layer of elastic tissue. The endothelial cells are thicker, shorter and broader than the cells which line the smaller vessels. The intermediate connective tissue, on which these cells rest, consists of a thin layer of fine elastic and collagenous fibers. The elastic fibers of this layer are continuous with the internal elastic membrane. This internal elastic membrane is composed of a network of elastic fibers arranged in the form of several fenestrated layers. Some of the elastic fibers from this layer combine with the elastic fibers of the media. Likewise, a few smooth muscle fibers from the media may penetrate this portion of the intima.

The *media* consists mainly of elastic tissue in the form of fenestrated membranes, between which the smooth muscle fibers are seen as relatively thin, flattened elements. The quantity of muscle in the media

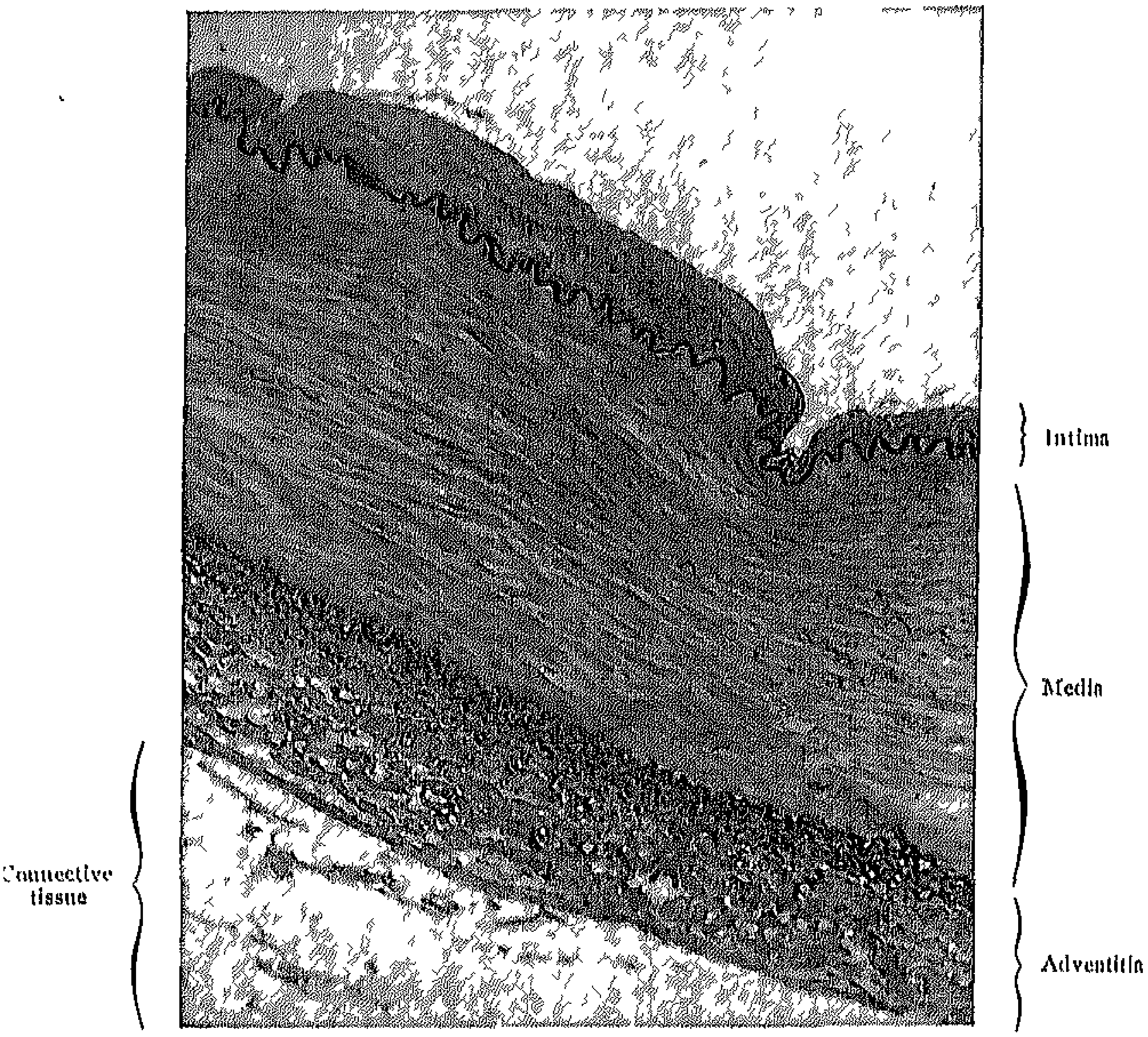


FIG. 97. Cross section of a muscular artery stained with resorcin-fuchsin. Photomicrograph

is greatly reduced compared to that in the muscular arteries, and the fibers are arranged in the form of a syncytium. The spaces between the muscle fibers and the fenestrated membranes are occupied by delicate elastic fibers with a few scattered collagenous fibers which serve to bind the structures together.

The *adventitia* is relatively thin, and consists of both elastic and collagenous tissue. These fibers, like the fibers of the media, pursue a spiral course around the vessel wall.

MUSCULAR ARTERIES. All named arteries, except those designated as elastic arteries, are classed as muscular arteries. Blood is conveyed to the muscular arteries by the elastic arteries. Muscular arteries are also known as *"distributing arteries"* and, as their name implies, their function is to carry blood to all parts of the body and to regulate (by relaxation or contraction of their walls) its distribution as the functional needs of the areas demand.

The *intima* consists of three well-defined layers, the endothelium lining the vessels, an intermediate layer consisting of a relatively thick layer of delicate collagenous and elastic fibers, and an internal elastic membrane. The internal elastic membrane is thick and well-developed in the larger medium-sized arteries. In some vessels it shows as a double membrane due to splitting of the layer. In the smaller vessels of this class the intima is considerably reduced, and in some cases the endothelium appears to lie directly on the elastic interna. The internal elastic membrane is thrown into folds by the development of a well-defined, thick, muscular media.

The *media* of these vessels is very thick. It consists of from 25-40 layers of smooth muscle fibers, arranged in layers which encircle the vessels. Longitudinally directed muscle fibers are not present in this layer. Elastic fibers are scattered throughout the media. The arrangement of the elastic tissue in the larger vessels of this group is in the form of fenestrated membranes not unlike those of the elastic arteries. In the smaller muscular arteries the elastic fibers are thinly scattered among the muscle fibers.

The *adventitia* of a muscular artery is relatively thick. It consists of collagenous and elastic fibers which are for the most part longitudinally directed. The elastic tissue, near the media, in the larger vessels is condensed to form an external elastic membrane. The fibers of the outer portion of the adventitia merge with the loose connective tissue by which the artery is surrounded. Occasionally throughout the adventitia longitudinally directed smooth muscle cells may be found.

ARTERIOLES. These small vessels are found between the muscular arteries and the capillaries. The flow of blood through these vessels is intermittent and is slower than in either the elastic or muscular arteries. Toward the larger end of the arteriole where it merges with the muscular artery, the coats are similar in structure to these vessels. This arrangement is found in arterioles of 400 microns or larger. In vessels ranging in size from 400–130 microns there is a gradual decrease in the number of muscle layers from a well-defined media to a media composed of only 3 or 4 layers of cells. The internal elastic membrane gradually thins down and becomes less distinct. In vessels of 130 microns, it is made up of elastic fibers forming a delicate meshwork. The adventitia likewise decreases in thickness. It is composed of elastic and collagenous fibers. The elastic fibers are arranged longitudinally and they tend to be concentrated in the region nearest the media. With the further decrease in caliber of these vessels the changes indicated above are progressively continued. The muscle layer is still further reduced in thickness until, in the *precapillary arterioles*, the muscle fibers no longer form a complete layer of cells, but rather are represented by single smooth muscle fibers encircling the vessels. The adventitia is reduced to a thin fibrous layer composed of a thin layer of collagenous fibers arranged longitudinally and containing scattered fibroblasts. A few elastic fibers are scattered throughout the walls of these small vessels, but a definite internal elastic membrane cannot usually be found in vessels with a diameter of less than 60 microns. While these layers become thin and ill-defined in the smallest arterioles, nevertheless, the three coats, the intima, media, and adventitia, can be identified.

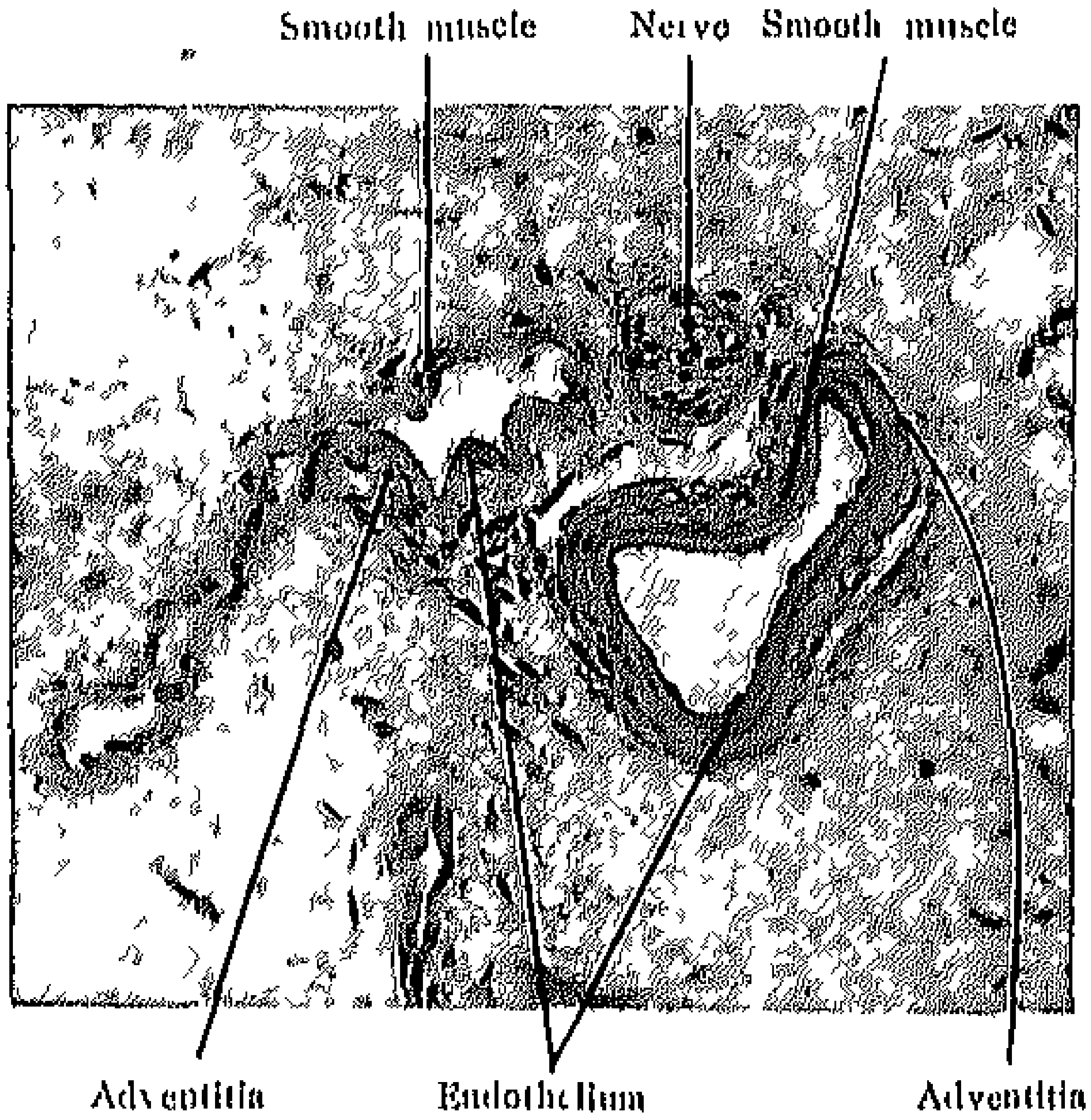


FIG. 98. Cross section through a small arteriole and venule. Photomicrograph.

CAPILLARIES. The capillaries are the smallest and most simply constructed vessels of the blood vascular system. Their diameter varies from 5–10 microns, the average being about 8 microns in man.

The capillaries branch freely, the branches anastomosing and forming complicated networks. Unlike the other vessels of the vascular system, the branches of the capillaries show little or no change in diameter. Moreover, the caliber of each branch is constant throughout its length. The capillary networks form meshes of various patterns and sizes in the different tissues and organs in which they are found. The density of the capillary network depends on the metabolic activity of the tissue. Wide meshes occur in areas where there is less need for a rich blood supply, as in dense areolar tissue. The meshes may be small and the capillary network very dense thereby forming a rich vascular supply. This arrangement is typical of the lungs and striated muscle.

Capillaries are merely endothelial tubes. When treated with silver nitrate, the boundaries of the endothelial cells appear as fine, dark, wavy or serrated lines. In the smaller capillaries, the walls may be formed of cells which are bent until their sides are in contact with one another. In the larger capillaries, two, three or more cells may be required to completely encircle the tube. Surrounding the endothelial tubes and accompanying them throughout their entire extent is a delicate layer of connective tissue (collagenous or reticular connective tissue). Also in close contact with the endothelial cells are fibroblasts, histiocytes, and undifferentiated mesenchymal cells of the connective

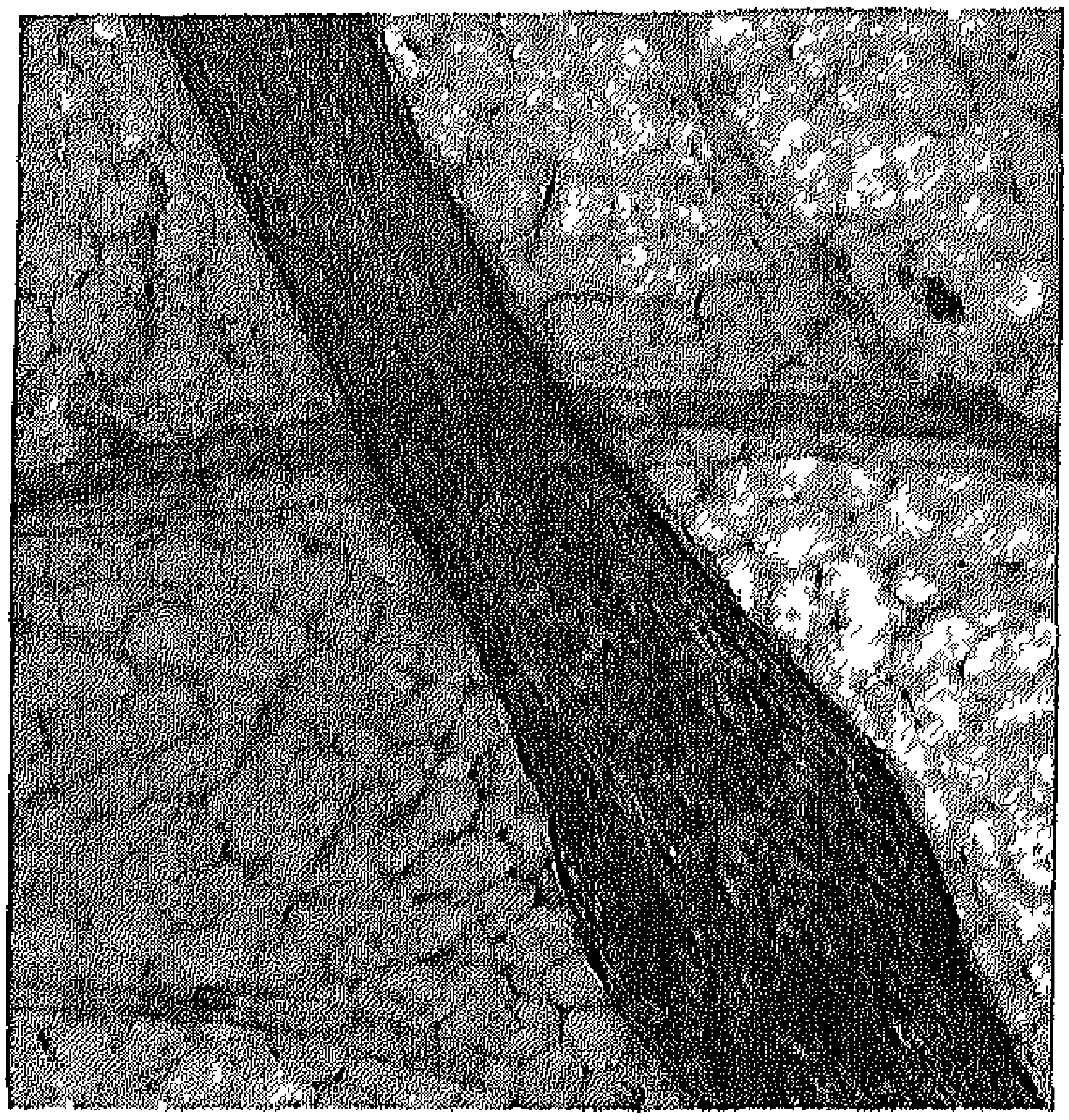


FIG. 99. Longitudinal view of small vein to show endothelial cells and valves. Note the swelling of the vein just proximal to the valve. Silver stain. Photomicrograph.

tissue layer. Another type of perivascular cell which has been described in relation to capillaries is the Rouget cell (first observed in the capillaries of the nictitating membrane of the frog's eye). These cells are considered by some to be elementary muscle cells and they are scattered along the entire extent of the capillary in an irregular fashion. Electrical stimulation causes them to contract. Rouget cells are elongated, irregular in shape, and have numerous slender, branching processes which encircle the capillary. The cell bodies and their processes contain fibrils which are thought to be the contractile elements of the cells. They are thought to assume the role of smooth muscle fibers in relation to the capillary wall, and transition forms between the Rouget cells and the smooth muscle fibers of the arteriole wall have been reported. However, these cells are not the only contractile elements found in relation to capillaries. Recent and careful observations made on the endothelial cells themselves have shown that these cells may also contract if they are subjected to mechanical stimulation. However, most of the contractile property of capillary walls is due, probably, to a passive contractility observed when the caliber of the vessels returns to normal after having been dilated by the blood forced into them from the arterioles.

The capillaries form an extensive area throughout the body. If all of the capillaries were open at one time, the area of this capillary bed would be sufficient to contain all the blood in the vascular system. However, only part of the capillaries are open to blood flow at one time, the remainder are collapsed and empty. The nutritional substances, brought to the tissues by the blood, pass through the walls of the capillaries into the tissue fluids. Waste substances, which are removed by the blood, also pass through these walls to enter the blood stream. Leucocytes enter or leave the blood stream (diapedesis) in the capillary area by pushing their way between the endothelial cells. Dilatation of the capillary increases the permeability of its wall.

SINUSOIDS. Sinusoids are thin-walled capillary vessels which occur in the liver, spleen, bone marrow and the ductless glands. They differ from capillaries in being wider and in not having a constant diameter; for example, a sinusoid which measures 10 microns at one point may have a diameter of 30 microns at another. The cells which form their walls are loosely attached and occasionally one may separate from the endothelium and float away in the blood stream. These cells possess marked phagocytic properties.

Variations of the diameter of the sinusoids in the liver and ductless glands are determined by the shape of the cords or masses of the parenchymal cells of the organ. Where the spaces between the parenchymal cells are narrow, the diameter of the sinusoid is correspondingly small; where the spaces are wider, the caliber of the sinusoid is increased. A thin layer of reticular tissue is interposed between the endothelial wall of the sinusoids and the parenchymal cells of the organ.

VEINS

The veins are the vessels (with the exception of the portal vessels and their tributaries) through which the blood passes from the capillaries to the heart. They can be distinguished from the arteries by their relatively thinner walls, the greater diameter of their lumen, and by their collapsed condition when empty. There is a decrease in muscular and elastic elements and an increase in the collagenous tissue in the walls of veins. The muscle layers are separated by many collagenous

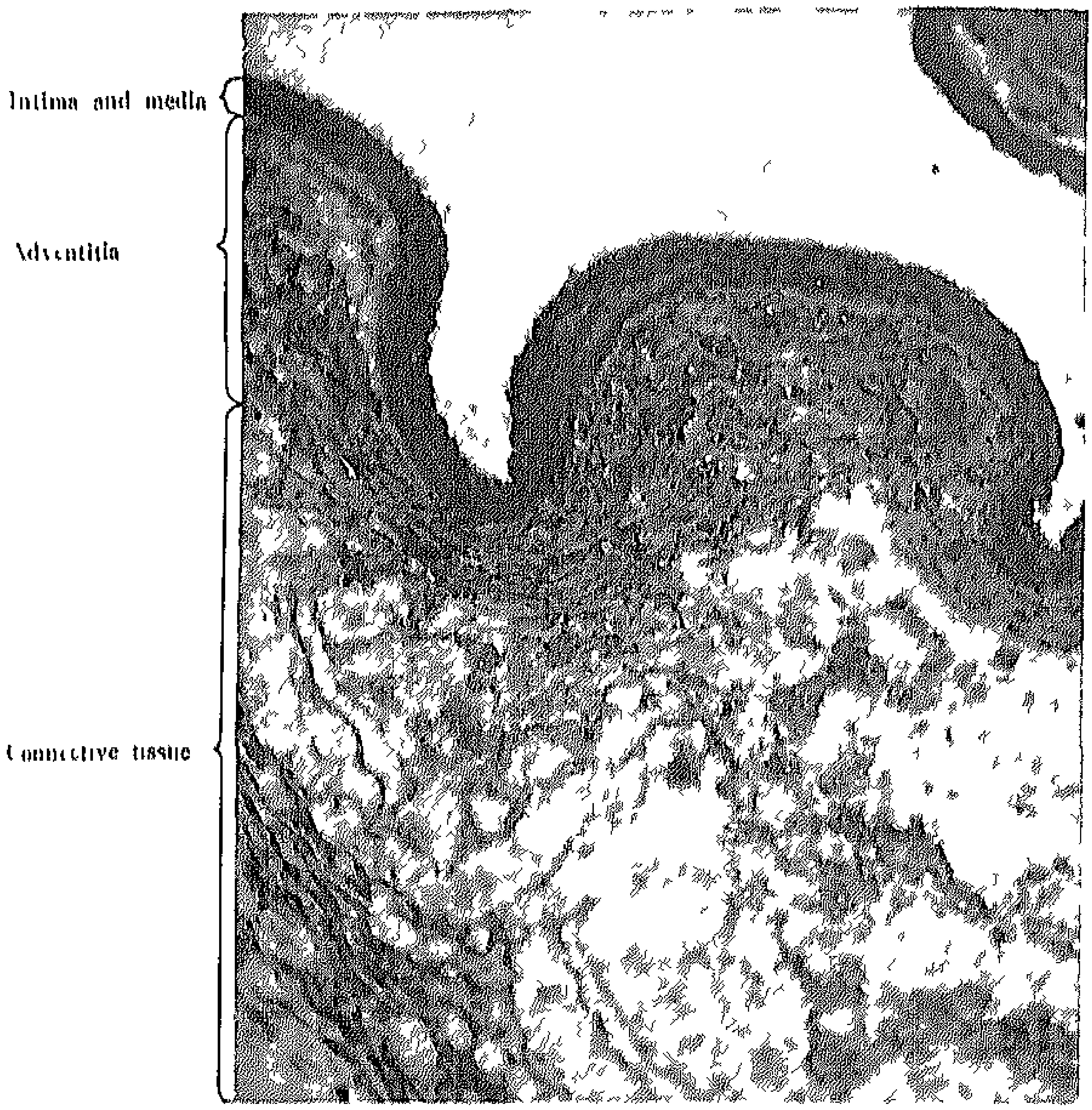


FIG. 100. Cross section of a large vein stained with resorcin-fuchsin. Photomicrograph

fibers and there is no distinct internal elastic membrane except in the larger veins.

The walls of veins, like those of arteries, consist of the three coats: intima, media, and adventitia. The development of these coats varies somewhat in veins of the same caliber in different localities.

VENULES. There is not a pronounced difference, either histologically or functionally, between capillaries and small venules. The venules are at first made up of endothelium surrounded by a thin layer of connective tissue. As in the walls of the capillaries, a considerable amount of exchange of substances between the blood and tissue fluids takes place in the venules. When the venules reach a diameter of about 45 microns, scattered smooth muscle fibers begin to appear. Venules of 0.2 millimeter diameter have a continuous muscular layer of circularly arranged fibers. A fairly thick adventitia is present and is composed of collagenous fibers arranged longitudinally. Elastic fibers are few and scattered.

With the increase in size of the veins, the muscle layer becomes thicker. These muscle fibers are arranged in layers which are separated from each other by collagenous tissue. Elastic fibers increase in number and a poorly organized internal elastic membrane is present.

MEDIUM-SIZED VEINS. In the medium-sized veins, the intima is thin. The endothelial cells are short and diamond-shaped. Beneath the endothelial cells is a layer of fine collagenous and elastic fibers. The internal elastic membrane is poorly developed; in the large veins it is represented by a network of elastic fibers.

The media is relatively thin and consists of layers of circularly arranged muscle separated by collagenous and elastic tissue. The media is best developed in the veins of the extremities. It is poorly developed in the veins of the viscera and of the head.

The adventitia is considerably thicker than the media. It consists of loosely interwoven collagenous fibers in which a number of longitudinal bundles of smooth muscle may occasionally be present.

LARGE VEINS. In the very large veins the quantity of circularly directed muscle is reduced and there is a marked increase in the longitudinally directed muscle fibers in the adventitia. The media is very thin and may be lacking entirely in places, particularly on the inner two-thirds, the outer one-third being chiefly collagenous fibers. In cases where the media is wanting (the venae cavae) these longitudinal fibers constitute the entire musculature of the venous wall.

VALVES OF THE VEINS. The tendency of the blood to flow backward in the veins, when acted on by gravity, is prevented by a series of structures, the *valves*. These are present in the medium-sized veins (those with a diameter over 2 millimeters), especially those of the extremities. The valves are folds of the intima which are attached to the inner walls of the vessels. They are usually located distal to the entrance of a branch into the vein. Each valve consists of two pouches located opposite to one another. When the blood settles back in these pouches, their free edges are pressed together and check the flow of the blood from the direction of the heart.

The valve consists of connective tissue covered by a continuation of the endothelial lining of the vessel. Elastic fibers are present in the connective tissue on the side toward the lumen, but are absent from the side of the valve which is toward the wall of the vein. Those veins in the body that do not have valves are: superior and inferior venae cavae and their tributaries, the umbilical vein, veins of the brain, spinal cord and the meninges.

ARTERIOVENOUS ANASTOMOSES

There are several places in the body where arterioles join directly to venules without any intervening capillaries. Such anastomoses occur:

in the palm of the hand, in the skin over the tips of the fingers, in the nail bed, and on the sole of the foot.

THE CAROTID BODY

The *carotid body (glomus caroticum)* is a small reddish body about the size and shape of a grain of wheat, which lies in or near the bifurcation of the common carotid artery. It consists of cords and masses of epithelioid cells arranged about relatively large vascular spaces. A dense fibrous matrix encloses the cellular and vascular components. There are no chromaffin cells present as was formerly believed and the latest evidence indicates that this structure is not, therefore, one of the paraganglia but rather a chemoreceptor or special sensory organ of the carotid artery. It is richly supplied with both myelinated and unmyelinated nerve fibers which terminate in relation to the epithelioid cells.

The *coccygeal body* is a somewhat similar structure which lies on the anterior surface of the coccyx. It differs from the carotid body in the origin of its cells, which are considered by some to be smooth muscle cells that have assumed an epithelioid appearance, and in the arrangement of its blood vessels. These vessels are extremely tortuous and communicate with the middle sacral artery. Although its structure suggests a possible endocrine function, its character as an endocrine gland has been denied.

BLOOD AND NERVE SUPPLY

The oxygenated blood, carried by the arteries, supplies the intima and the inner portion of the media. The remainder of the arterial wall is supplied by vessels located in the adventitia. These vessels give off branches which penetrate the outer portion of the media in the larger vessels. The veins, which carry nonoxygenated blood, are supplied with vessels which penetrate the media, and in the larger veins, may even enter the intima. Vessels which carry blood to the walls of arteries and veins are known as *vasa vasorum.*

The walls of the blood vessels are supplied with both motor and sensory nerve fibers. The motor fibers are from the sympathetic system, and are of two kinds: fibers which convey impulses that cause a lessening of the caliber of the vessel, the *vaso-constrictor fibers;* and those which cause dilation of the caliber of the vessels, the *vaso-dilator fibers.* Myelinated fibers carry sensory impulses from the walls of the vessels.

THE HEART

The heart is a large muscular organ located in the *mediastinum,* a division of the thoracic cavity. It is enclosed by a fibrous sac, the *pericardium,* and consists of four chambers: the *right* and *left atria* and the *right* and *left ventricles.*

The heart may be regarded, structurally, as an expanded or overgrown artery and vein placed side by side. The right side, which has the thinner wall and receives venous blood, representing the venous component; the left side, having the thicker wall and receiving arterial blood, representing the arterial component. The endocardium would correspond to the intima, the myocardium to the media, and the epicardium to the adventitia.

The heart wall consists of three layers: an internal layer, the *endocardium;* a greatly thickened muscular layer, the *myocardium;* and an external fibrous layer, the *epicardium.*

The endocardium consists of a layer of endothelial cells supported by a thin substratum of very fine collagenous fibers, which rests on a thicker layer of mixed collagenous and elastic fibers in which a few smooth muscle fibers may be found. It is continuous with the intima of the arteries and veins.

The myocardium is the muscular portion of the heart wall. It consists of fibers of cardiac muscle, partially separated into bundles by septa of connective tissue, the bundles being arranged in layers. In the atrial wall the fibers of the superficial layer encircle both atria, while the fibers of the deep layer have a longitudinal arrangement in each atrium. The muscular layers of the ventricles begin with their attachment to the dense fibrous rings *(annuli fibrosi),* the superficial layer looping around both ventricles, the fibers of the deep layer passing through the interventricular septum and encircling a single ventricle. The fibers of both layers end in the papillary muscles on the side opposite their origin.

The epicardium is formed by the visceral layer of the pericardium and is attached to the external surface of the myocardium. The serous membrane, which forms its outer layer, is separated from the myocardium by a layer of collagenous and elastic fibers. This layer is thickened and covers the coronary arteries and their branches as they lie in furrows on the surface of the heart. Considerable accumulations of fat are formed in these thickened areas. The septa, which lie between the partially formed bundles of cardiac muscle, are continuous with both the epicardium and the endocardium and form a framework by which the myocardium is supported.

VALVES OF THE HEART

Between the atria and the ventricles are rings of dense fibrous tissue, the *annuli fibrosi,* which provide the principal support for the tissues of the heart. Attached to these rings and extending into the ventricles are fibrous flaps or cusps which form the atrioventricular valves. These valves are arranged so that when the ventricles contract, blood is not forced back into the atria. The free borders of the cusps are attached by fibrous cords *(chorda tendineae)* to muscular projections from the walls of the ventricles *(papillary muscles)*.

ATRIOVENTRICULAR VALVES. The atrioventricular valves are membranous flaps which extend from the borders of the atrioventricular openings into the ventricles. The valve on the right side consists of three flaps or cusps *(tricuspid valve)*; that on the left consists of two cusps *(bicuspid* or *mitral valve)*. The cusps of the atrioventricular valves are attached to the fibrous rings about the atrioventricular openings. They are somewhat thickened at their roots, becoming thinner toward their free margins. They consist of fibrous tissue, extending from the fibrous rings, and an outer covering of endothelium which is continuous with that forming the lining of the heart. The endothelial cells are thickened on the atrial side of the valve, and rest on a layer of condensed connective tissue which has almost the consistency of cartilage. The tissue immediately beneath this layer consists of closely interwoven elastic fibers. The connective tissue on the ventricular side of the valve is more loosely arranged and contains fewer elastic fibers. Scattered smooth muscle fibers are present in the valve on the atrial side. Bundles of cardiac muscle extend for some distance into the root of the valve. The *chorda tendineae* are composed of collagenous and elastic fibers which extend from the margins and ventricular surfaces of the cusps to the papillary muscles.

SEMILUNAR VALVES. Pocketlike valves that are larger, but otherwise similar to the valves described for the veins, are located at the roots of the pulmonary artery and aorta *(semilunar valves)*. Their function is to prevent the blood from returning to the ventricles when the latter are expanding.

Each semilunar valve consists of three pocketlike cusps arranged about the openings from the ventricles into the pulmonary artery and aorta. The structure of the cusps is similar to that of the atrioventricular valves, except that the thicker endothelium and network of elastic fibers are on the ventricular side. There is also no extension of muscle from the myocardium into the valves. The connective tissue is accumulated at the middle of the free border of each cusp and forms a rounded projection, the *fibrous nodule*.

IMPULSE CONDUCTING SYSTEM

In addition to an innervation by way of the vagus and the sympathetic nerves, the heart has a specialized neuromuscular apparatus known as the *impulse conducting system (bundle of His)*. The function of this system is to coördinate the contractions of the atria and ventricles.

This conduction system of the heart consists of specialized muscle fibers known as *Purkinje fibers*. They form a complex network beginning in the right atrium near the entry of the venae cavae and spread throughout the entire heart, extending into the atria as well as the ventricles. In the atria where the musculature of the walls is somewhat reduced, the Purkinje fibers are concentrated in a small area known as the *atrioventricular node.* Similar areas where the fibers can be more readily identified and demonstrated are known as the *sinoauricular node* and the *bundle of His.* Because of this, these three structures have been singled out, studied and described. This has resulted in the formation of an erroneous conception of the extent and distribution of the conduction system.

As usually described the sinoauricular node is located in the subepicardial tissue at the point where the superior vena cava joins the right atrium, near the sulcus terminalis. From here fibers spread into the myocardium of the right atrium. The atrioventricular node is located in the interatrial septum, principally on the right side in the vicinity of the coronary sinus. From the atrioventricular node the fibers converge to form the bundle of His, which extends into the membranous portion of the interventricular septum, where it divides into two main branches. These branches pass to the ventricles, in the walls of which they break up into numerous fine subdivisions which are distributed among the fibers of the myocardium.

The sinoauricular node is thought to initiate the stimuli producing cardiac contraction, hence, it is called the pacemaker of the heart. From here the wave of contraction spreads throughout the atria by way of typical cardiac muscle fibers. The impulse reaches the atrioventricular node and from there it extends along the bundle of His and its branches to the cardiac muscle fibers of the ventricles.

Purkinje fibers are made up of Purkinje cells laid end to end. The appearance of these cells has been carefully studied in human hearts by Todd who gives a rather detailed description of two distinct types with intermediate forms. He also describes transitional forms between true cardiac cells and Purkinje cells.

The adult Purkinje cells make up the greater part of the conducting system of the heart. These cells are laid end to end and thus form the Purkinje fibers. These cells are large and possess more cytoplasm than ordinary cardiac muscle cells. The myofibrillae are reduced in number, and are located about the periphery of the fibers. These cells show both longitudinal and cross striations, however, the latter are more faint than those of cardiac muscle. Intercalated discs cross the fibers at irregular intervals. A fine connective tissue *(endomysial membrane)* surrounds the individual Purkinje fibers. Bundles of fibers are enclosed by a sheath of connective tissue by which they are separated from the myocardium. The presence of this system in human hearts has been seriously questioned by Glomset.

BLOOD AND NERVE SUPPLY

The wall of the heart is supplied with blood by two coronary arteries which arise from the root of the aorta (aortic sinuses). The branches of these coronary arteries spread out over the surface of the heart and their subdivisions penetrate the myocardium where they break up into capillaries which are distributed to the muscle fibers. Blood is returned from the heart wall through the coronary veins which unite to form a large, thin-walled coronary sinus which opens into the right atrium. In addition, there are Thesbian veins which open directly into the right atrium.

The heart receives nerves from the vagus and the sympathetic division of the autonomic system by way of the cardiac plexus. The vagal parasympathetic fibers end in relation to ganglion cells in the epicardium from which postganglionic fibers penetrate the myocardium to end in relation to the muscle fibers. The cardiac nerves carry the sympathetic fibers which terminate in cardiac musculature and in the smooth muscle of the wall of the coronary vessels. Fibers from the vagus transmit depressor impulses, while those from the sympathetic system transmit accelerator impulses.

THE LYMPHATIC SYSTEM

The lymphatic system is peculiar in that it does not form a complete circulatory circuit. Rather, it begins in blind-end capillaries in the peripheral areas and the direction of the flow is toward the heart. The capillaries form an extensive network in practically all of the tissues of the body, however, lymph vessels have not been found in the central nervous system or in the endoneurium of peripheral nerves. They are absent also in the parenchyma of the spleen, endomysium of striated muscle, the coats of the eyeball and the internal ear.

The lymph capillaries are slightly larger than those of the blood vascular system, and owing to the thinness of their walls and their collapsed condition, cannot be distinguished from the surrounding tissues in ordinary preparations. In the intestinal villi the lymph capillaries are in the form of simple, saclike extensions which are called *lacteals,* owing to the milky appearance of their contents when they have collected the digested fats.

The walls of the lymph capillaries are formed by thin, flattened endothelial cells. When their outlines are made visible by the application of silver nitrate, the cells are seen to bear a close resemblance to the endothelial cells which line the blood vessels.

The capillaries unite to form the smaller *lymph vessels* which, in turn, combine to form the larger vessels. The walls of the smaller vessels consist of endothelium about which are longitudinally arranged

DIFFERENTIAL STRUCTURAL CHARACTERISTICS OF BLOOD VESSELS

Name of Vessel	*Intima*			*Media*		*Adventitia*
	Endothelium	*Collagenous Fibers*	*Elastic Tissue*	*Elastic Tissue*	*Smooth Muscle*	
Elastic arteries	Present	Thin, dense layer	Present as fenestrated layer	Abundant as fenestrated layers	Present, not abundant	Relatively thin layer. contains smooth muscle
Muscular arteries	Present	Present	Present as an internal elastic membrane	Present but less abundant than in elastic arteries	Present in relatively large amounts	Whole layer relatively thick
Arterioles	Present	Absent	Very little or none	Very little or none	Relatively largest amount of any vessel	About as thick as the media
Capillaries	Present	Absent	Absent	Absent	Absent or only occasional fibers Rouget cells present	Absent or extremely thin
Venules	Present	Present in small amounts	Present but poorly developed	Present	Present in scattered bundles	Moderately thick layer
Veins	Present	Present in moderate amounts	Present in form of network	Present but not abundant	Present in moderate amounts	Relatively thick layer (thicker than media) and contains smooth muscle

collagenous and elastic fibers (no Rouget cells are present), with a scattering of smooth muscle fibers. In the larger lymph vessels, the longitudinally directed collagenous and elastic fibers form a layer which corresponds to the intima of the blood vessels. External to this is a muscular coat which corresponds to the media. The inner layer of smooth muscle fibers is circularly arranged, the fibers of the outer layer being more or less oblique in direction. The adventitia consists of both collagenous and elastic fibers, in which a few longitudinally directed bundles of smooth muscle may be observed in the larger vessels.

The lymphatics are supplied with valves, which are closer together than in the veins. These valves consist of endothelium supported by connective tissue, both of which are extensions of the intima. The walls of the lymphatics are expanded in front of the valves, which gives the vessels a beaded appearance.

The lymph vessels empty into two large *lymph trunks* or *ducts:* the *right lymphatic duct* and the *thoracic duct*. The right lymphatic duct is a short vessel which receives the lymph from the right arm and shoulder and the right side of the head and neck. It joins the blood vascular system at the junction of the right internal jugular and subclavian veins. The thoracic duct begins a short distance below the diaphragm in an enlargement, the *cisterna chyli*. It passes upward through the thorax into the root of the neck, where it joins the blood vascular system at the junction of the left internal jugular and subclavian veins. It receives lymph from the left arm and shoulder, the left side of the head and neck, the trunk and the lower extremities.

The walls of the large lymphatics are supplied with blood vessels similar to the vasa vasorum of the arteries and veins.

The nerve supply is from the autonomic system and is distributed to the muscle fibers. A few fibers, possibly sensory in function, penetrate the intima.

12

Lymphoid Organs

Reticular connective tissue is widely distributed throughout the body. In the mucous membranes it lies between the epithelium and the layer of collagenous and elastic fibers which form the submucosa. In some localities reticular tissue forms a thin and not readily discernible layer, as in the membranes lining the oral cavity, the respiratory passages, etc. In the alimentary canal this tissue constitutes a layer of considerable thickness, the tunica propria.

Reticular connective tissue, wherever it occurs, even when it is not readily observed, is indicated by the presence of lymphocytes. These cells are especially numerous in areas where the tissue is abundant. The manner in which lymphocytes are assembled varies with the locality and the amount of reticulum present. Where the reticular tissue forms a relatively thin layer, the lymphocytes are more or less scattered. This is known as *diffuse* lymphoid tissue. In areas where the reticulum is more abundant, the lymphocytes may be crowded together in irregular masses, the *aggregate* type of lymphoid tissue. In other areas, lymphocytes may form aggregations which present a more or less definite or circumscribed outline when seen in sections. Such bodies are known as *lymph nodules*. When fully developed, lymph nodules possess a lighter central area known as a *germinal center*. The presence of the germinal center is not constant, but is correlated with the functional activity of the nodule. In the germinal center the lymphocytes are larger and are not as closely crowded as in the darker area by which it is surrounded. The meshes of the supporting reticular network are wider in the germinal center than in the adjacent parts of the nodule. The coarser meshes in the center permit the lymphocytes to separate from one another, while the finer meshes of the reticulum at the periphery of the nodule hold the lymphocytes in a more compact mass.

Lymph nodules may appear singly *(solitary nodules)*, or in groups *(aggregated nodules; agminated glands)*, as in Peyer's patches in the lower portion of the small intestine. Lymphoid structures of this type are not separated from the surrounding tissues by connective tissue capsules. Encapsulated aggregations of lymph nodules form the so-called lymphoid organs. These are the *lymph glands (lymph nodes)*, the *spleen*, the *thymus*, and the *tonsils*.

LYMPH GLANDS

Lymph glands are small bodies varying from a millimeter to two centimeters, or more, in length. They occur in connection with the lymph vessels in various parts of the body. In certain localities, such as the cervical, axillary and inguinal regions, they occur in groups. These groups are known as the cervical, axillary or inguinal glands according to their location. Lymph glands are especially numerous in the mesentery, where they occur in connection with the mesenteric lymph vessels.

A lymph gland is a somewhat flattened, bean-shaped body with an indentation, the *hilum*, on one of its borders. The arteries enter and veins and lymph vessels leave the gland at the hilum. The parenchyma of the gland is invested by a dense connective tissue capsule which is somewhat thicker at the hilum. The capsule consists of compactly arranged collagenous fibers with scattered elastic fibers. The elastic fibers become more plentiful in the inner part of the capsule. From the capsule are given off, at right angles, connective tissue *trabeculae* or septa which extend into the outer or cortical portion of the gland

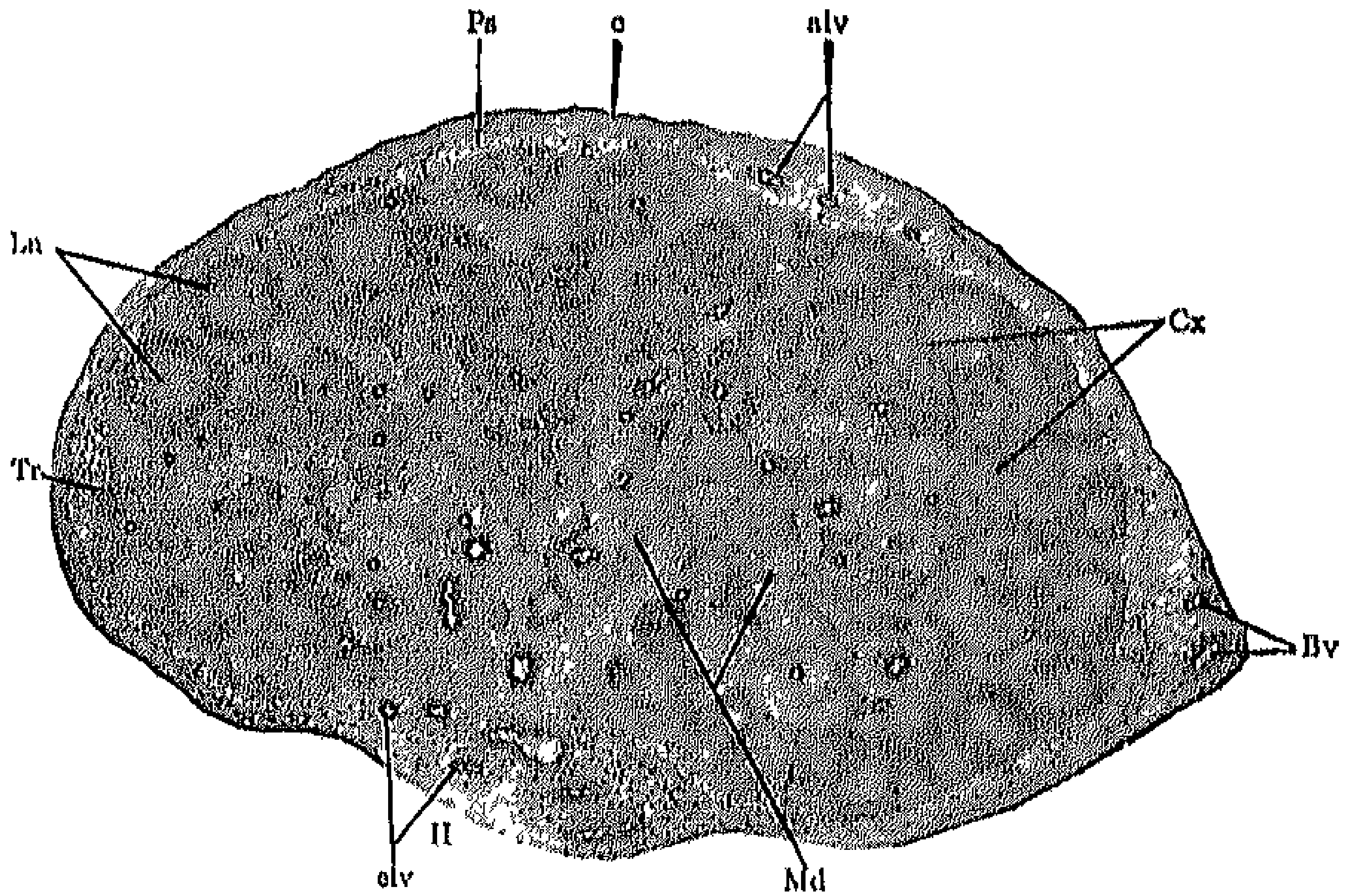


FIG. 101. Section through a lymph node. (c) Connective tissue capsule. (Ps) Peripheral sinus. (Cx) Cortex. (Md) Medulla. (H) Hilus. (alv) Afferent lymph vessels (elv) Efferent lymph vessels. (Ln) Lymph nodules showing germinal centers. (Tr) Trabecula extending from the capsule into the cortex.

and incompletely divide it into compartments. In the inner or medullary part of the gland these trabeculae branch and anastomose to form irregular spaces. Communications exist between the compartments of the cortex and between the cortical compartments and those of the medulla. The connective tissue of the capsule also extends into the gland at the hilum.

The compartments and spaces between the trabeculae are occupied by lymphoid tissue. This consists of reticular fibers which form the principal framework of the gland, and the numerous lymphocytes with which the meshes of the reticulum are filled. Toward the periphery of the gland the lymphoid tissue forms one, two, or more nodules in each compartment, however, not all of the lymph nodules show a germinal center. The portion of the gland between the lymph nodules is filled with diffuse lymphoid tissue. The nodules and the diffuse lymphoid tissue by which they are surrounded, constitute the *cortex* of the gland.

The diffuse lymphoid tissue is continued into the middle of the gland in the form of branching and anastomosing cords which enclose a number of open lymph spaces. These spaces are not separated from the cords by an endothelial lining, but are simply areas in the lymph gland from which lymphocytes are absent, and in which portions of the supporting reticulum may be visible. These spaces communicate with one another and converge toward the hilum. The portion of the lymph gland which is occupied by the cords of diffuse lymphoid tissue is called the *medulla*. The medulla is surrounded on all sides by the cortex, except at the hilum.

The capsule does not lie directly on the parenchyma, but is separated from it by a space, the *peripheral sinus*. The sinus extends into the substance of the gland on both sides of the trabeculae, and communicates with the lymph spaces in the medulla. Reticular fibers may be seen crossing the sinus from the capsule and trabeculae to the parenchyma.

The gland is supplied with both *afferent* and *efferent* vessels. A number of afferent vessels penetrate the capsule and open into the peripheral sinus. Unlike the blood vascular system which consists of a "closed" system of vessels, the lymph system is an open system and the lymph which is brought to the gland by the afferent vessels circulates freely throughout the sinuses of both the cortex and the medulla. The medullary sinuses give rise to a number of small vessels which pass toward the hilum. At the hilum these vessels join to form the efferent vessels.

An artery, which enters at the hilum, divides into branches, some of which go to the lymphoid cords of the medulla, the others continue in the trabeculae. The vessels to the medullary cords, after sending fine branches to these structures, continue into the cortex where they end in a network of capillaries in the nodules. The arteries entering the trabeculae supply blood to the connective tissue of the trabeculae and to the capsule, which they also invade. Branches from the trabecular arteries *pass through the lymph sinuses* to enter the parenchyma, where they terminate in capillaries in the lymph nodules. The blood returns in veins which follow the course of the arteries to the hilum where they unite to form a single vein that leaves the gland at this point. The vessels do not communicate with the lymph spaces, but form a closed system in the gland.

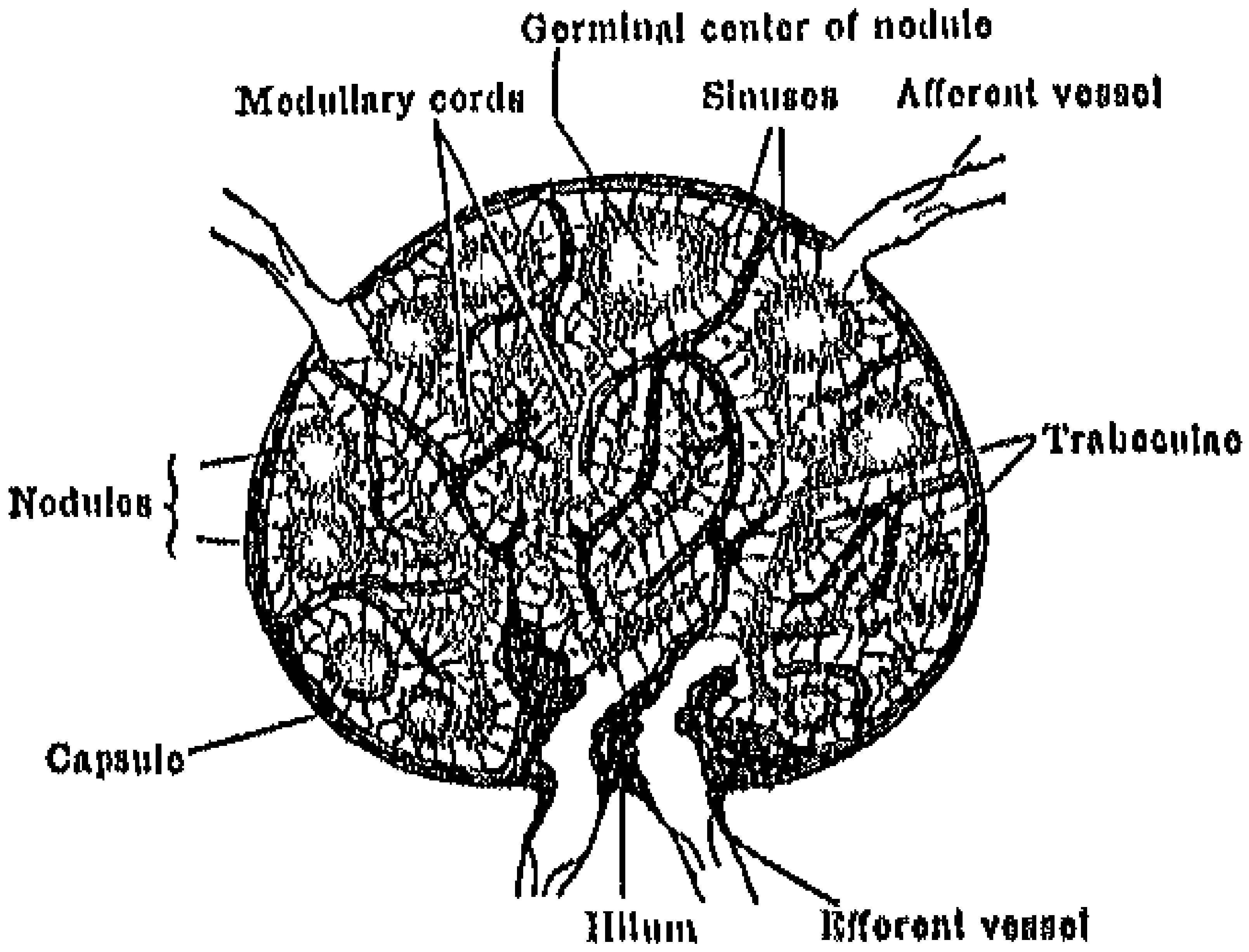


FIG. 102. Diagram of a lymph gland. The vascular supply is not shown. Arteries usually enter and the veins leave the organ at the hilum. (Courtesy, Cole: "Comparative Histology," Philadelphia, The Blakiston Company.)

The nerves are from the autonomic system. They enter at the hilum and are distributed mainly to the walls of the blood vessels.

Lymph glands perform two important functions: first, the production of lymphocytes; second, the removal of bacterial organisms and particulate matter, which may be brought into them in the lymph. This phagocytosis is carried on by the macrophages and the reticular cells which have retained their phagocytic properties.

The cells which are to be observed in the parenchyma of a lymph gland are those which belong to the reticulum, together with small, medium-sized, and large lymphocytes, and macrophages. There are two distinct types of cells forming the reticulum, phagocytic and nonphagocytic. The latter are similar to the undifferentiated mesenchyme cells and can give rise to reticular cells proper and to lymphocytes. The other cell type is the reticular cell proper which is definitely phagocytic

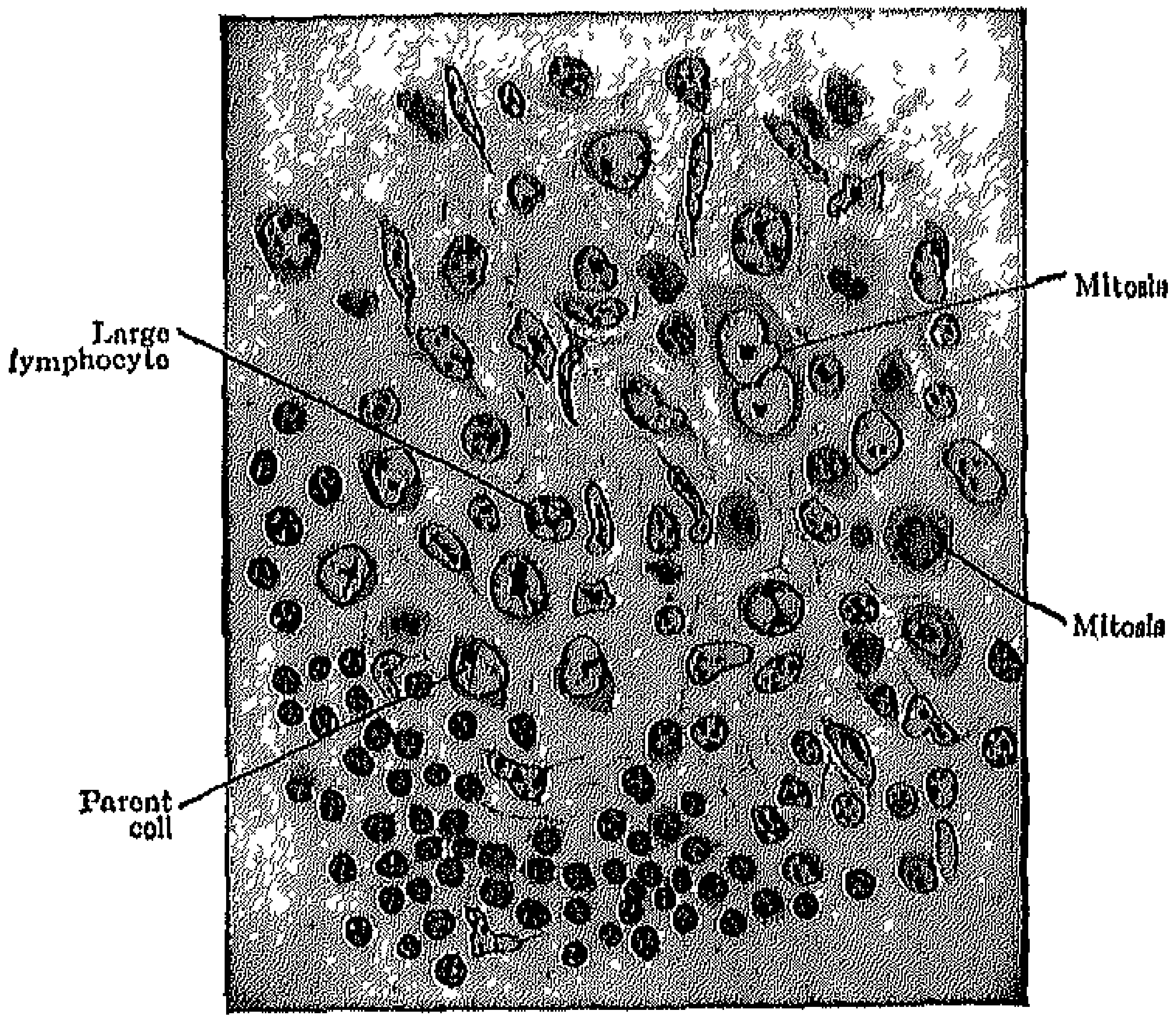


FIG. 103. Germinal center of human lymph node. Large clear cells resembling promyelocytes may be seen within the meshes of the reticular tissue; transitional forms of large and small lymphocytes may be seen. Cells frequently show mitotic figures. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

and is a part of the reticulo-endothelial system. These cells may become detached from the syncytium of which they are a part and become free macrophages. A few plasma cells, granulocytes and red corpuscles are found as free cells scattered throughout the parenchyma of the gland. These cells have probably entered by way of the blood stream. The small lymphocytes form the majority of the cells.

They are most abundant in the part of the nodule which surrounds the germinal center and in the diffuse tissue between the nodules. The medium-sized and large lymphocytes are most abundant in the germinal centers. The frequent presence of mitotic figures in these cells indicates an extensive cell proliferation in this region. The macrophages resemble the lymphocytes, except that they are larger and are provided with a nucleus which is not as densely chromatic. They are to be found in the germinal centers and in the lymph spaces and sinuses. Reticular cells are to be identified in the lymph spaces by their association with the fibers of the reticulum.

There is a considerable disagreement concerning the relationships of the cells in the lymph gland. The most commonly accepted view is that the undifferentiated reticular cells leave their position in the reticulum and divide, producing the medium-sized lymphocytes which, by continued division, produce the small lymphocytes. By a process of growth, the small cells become medium-sized and large and they are able to divide, small lymphocytes being the products of this division. Small lymphocytes are also derived from the large lymphocytes, the "lymphoblast" of the dualists and polyphyletics.

HEMOLYMPH GLANDS

Hemolymph glands are similar to lymph glands in their general appearance, except that they are a deep red color, resembling small clots of blood in the tissues in which they occur. They are found around the roots of the mesenteric arteries, in the region of the renal vessels and in association with the lymph glands in the mesenteries. The great variations in the size and structure of hemolymph glands has led to a considerable difference of opinion regarding their character. The presence of these structures has been described in some of the smaller animals (sheep and pig). It is doubtful if real hemolymph nodes occur in man. Glands which have been reported as hemolymph glands are now thought possibly to be simply lymph nodes in which hemorrhage has occurred either within the gland or in relation to the afferent vessels and the red blood cells have been brought in by one of these afferent vessels.

A typical hemolymph gland resembles a lymph gland in its form and general structure. It is invested by a connective tissue capsule, from which trabeculae extend into the gland. The parenchyma is divided into a cortex and medulla, in both of which the lymphoid tissue is greatly reduced in amount. Nodules, with germinal centers, are usually present in the cortex. Both afferent and efferent lymph vessels are wanting, the blood vessels communicating directly with the sinuses. Thus both the sinuses and lymph spaces are filled with red corpuscles. The presence of macrophages with pigmented cytoplasm indicates that the worn-out red corpuscles are disposed of in the hemolymph glands, by the phagocytic action of these cells.

THE SPLEEN

The spleen has been regarded by some investigators as an overgrown hemolymph gland, which it more nearly resembles in its general structure than it does a lymph gland. It differs from the lymph gland in that it has no afferent lymph vessels, neither does it have lymph-filled sinuses. The sinuses in the spleen are filled with blood. The spleen is five or more inches in length, about four inches in width, and is located to the left of and a little behind the stomach. Its substance is soft and pliable, so that it is easily moulded by contact with adjacent structures. The surface of the spleen, toward the wall of the stomach, presents an indentation, the *hilum*, at which point the splenic vessels,

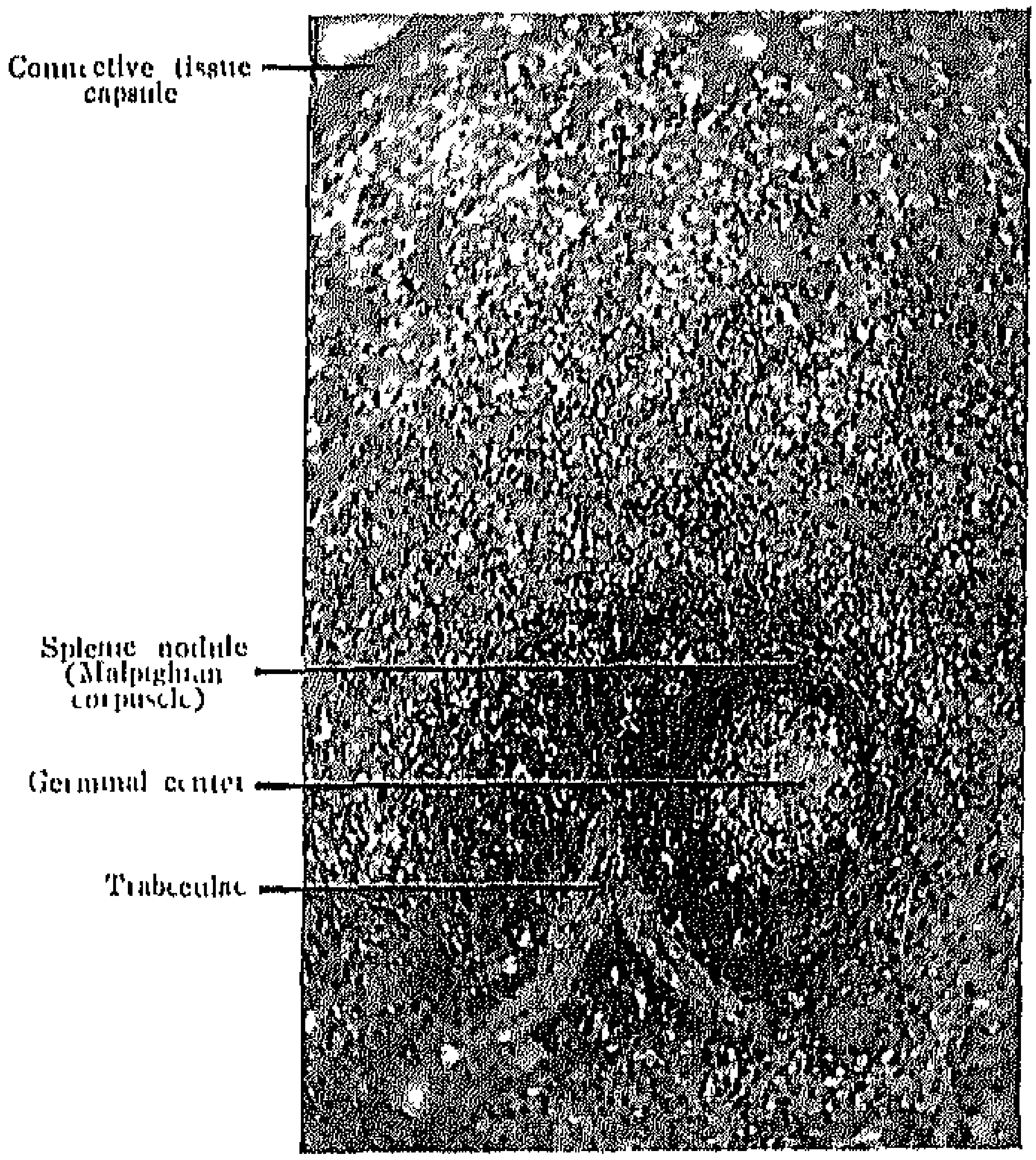

Connective tissue capsule
Splenic nodule (Malpighian corpuscle)
Germinal center
Trabeculae

FIG. 104. Section through a human spleen. Photomicrograph.

supported by connective tissue from the capsule, enter and leave the organ.

The parenchyma of the spleen is enclosed by a connective tissue capsule. External to the capsule is a thin layer of loose connective tissue covered by mesothelial cells (peritoneum) which forms a serous investment for the organ as far as the hilum. Here the serous membrane is reflected away from the spleen and is continuous with the peritoneal lining of the abdominal cavity. From the inner surface of the capsule, trabeculae extend into the substance of the organ and furnish the main support for the reticular tissue that forms the framework by which the parenchyma of the spleen is supported. These trabeculae branch and the branches anastomose, thus incompletely dividing the organ. The capsule and trabeculae are composed of many elastic fibers interwoven with collagenous fibers, and scattered small bundles of smooth muscle. Since the spleen is subject to considerable change in size, the large quantity of elastic tissue and smooth muscle in the capsule allows it to stretch to accommodate to this variation in volume.

The reticular tissue between the trabeculae forms the stroma and supports the splenic pulp. The pulp consists of a variety of cellular elements, among which the red blood corpuscles and lymphocytes form the predominant constituents. The lymphocytes have their origin in the lymphoid tissue of the spleen. A large number of cells known as *splenic cells (splenocytes)*, together with a few granulocytes and plasma cells, are also present.

The splenic cells or splenocytes, once thought to be characteristic of the spleen, are now believed to be identical with the monocytes which are produced in the spleen or those brought into the spleen by way of the blood stream. They are intensely phagocytic, and ingest not only fragments of worn-out red corpuscles, but entire corpuscles as well. In their larger forms, these cells bear a close resemblance to free macrophages. It is quite probable that the monocytes, or splenic cells, not only enter the spleen in the blood stream, but that they are also derived, by division, from the phagocytic reticular cells or from lymphocytes. In this case, they would be related to the lymphocytes on the basis of their origin. No clear evidence has yet been produced to disprove their lymphatic origin.

Numerous sinusoidal capillaries extend throughout the parenchyma of the organ and separate the pulp into cordlike masses, the *splenic cords*. Within the pulp cords there are compact masses of lymphocytes arranged in relation to blood vessels (branches of the trabecular arteries). At a number of points along the arteries the lymphocytes of the white pulp are in the form of nodules, and are known as *splenic nodules* or *Malpighian corpuscles*. Germinal centers may or may not be present. The number of germinal centers present decreases with age. The arteries around which these corpuscles are organized are not centrally located but tend to be eccentric in relation to the nodular tissue. Nevertheless, the arteries are referred to as the *central arteries*. Two arteries are frequently present in places where the nodule is formed about the bifurcation of a vessel. In splenic nodules the adventitia of the arteries is replaced by a reticular tissue in which there is an extensive proliferation of lymphocytes. The remainder of the pulp is composed of diffuse lymphoid tissue in which there are numerous red blood cells. This is known as the *red pulp* of the spleen.

The blood supply is by way of the splenic artery, which enters the spleen at the hilum. Branches of the splenic artery enter the trabeculae and are now known as *trabecular arteries*. These arteries continue for a short distance in the trabeculae before they leave to enter the substance of the pulp. In the pulp the adventitial coat is replaced by a reticular tissue layer into which lymphocytes filter to form the splenic nodules. In their relation to the nodules of the white pulp the arteries are known as *central arteries*. On leaving the nodules the arteries enter the red pulp and divide into a number of long, delicate branches which are called *penicilli*, because of their brushlike appearance. Each long branch of the penicillus has three portions. In order, they are called the *pulp artery, sheathed artery*, and the *terminal arterial capillaries*. The pulp arteries are longer than either of the succeeding arterial portions. The tunica media of the pulp arteries is made up of smooth muscle which is in direct contact with the red pulp. These vessels divide to form the sheathed arteries, which are enveloped by spindle-shaped sheaths, formed by the modification of the reticular tissue surrounding the vessels. The reticular cells and fibers form a concentrically arranged mass of tissue about the vessels which is known as the *sheath of Schweigger-Seidel*. The lumen of the vessel is narrowed as it passes through the sheath, an arrangement which is evidently a device for reducing the volume of the blood that enters the terminal arterial capillaries. The sheaths do not possess muscle fibers and appear to exist for the purpose of enabling the wall of the artery to resist the increased pressure at this point. Beyond the sheaths, the arteries break up into their terminal branches (terminal

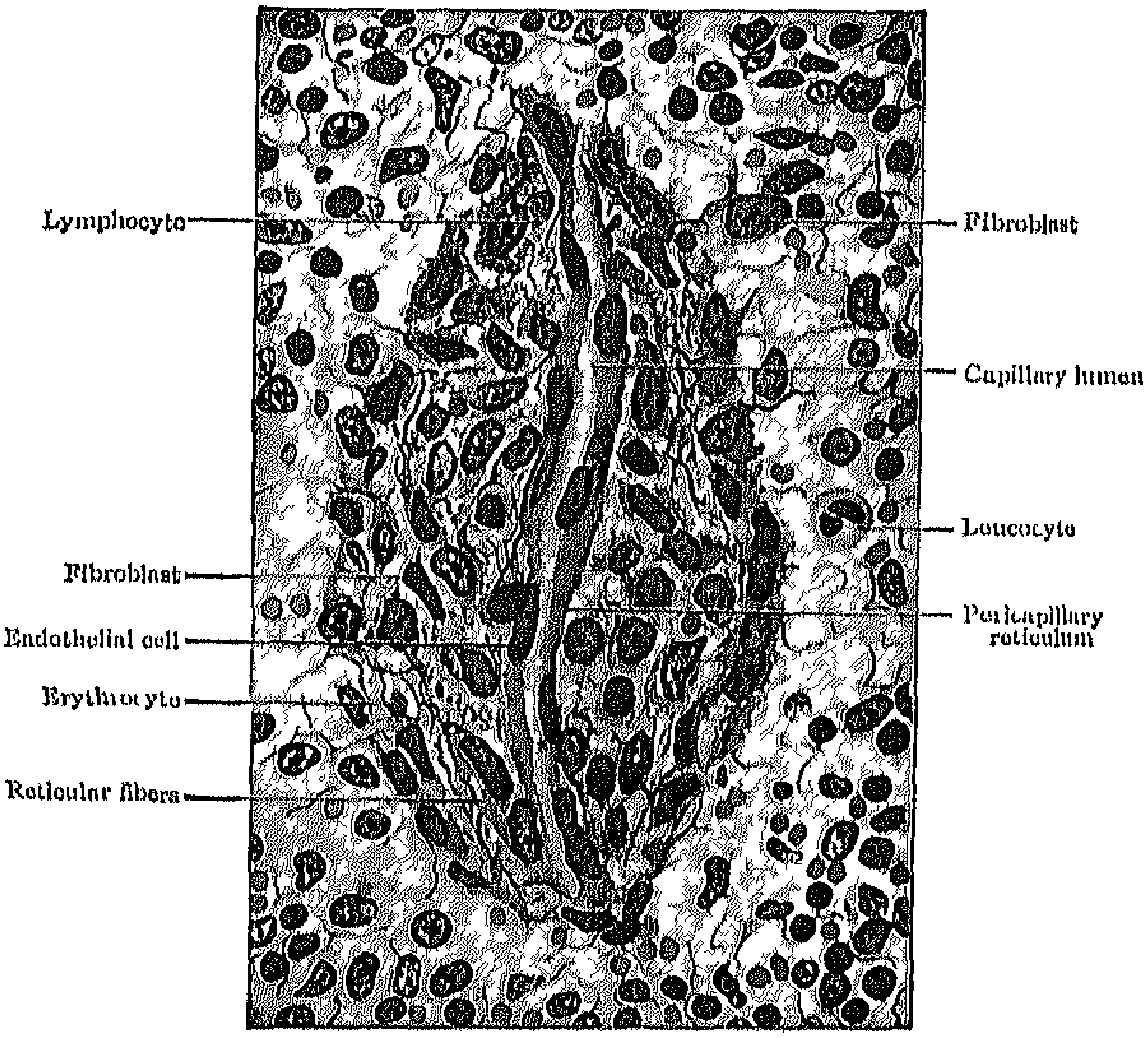


FIG. 105. "Sheathed artery" in the spleen of a cat. Contracted organ. Susa fixation; eosin-methyl blue. 800 ×. (Riedel.) (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

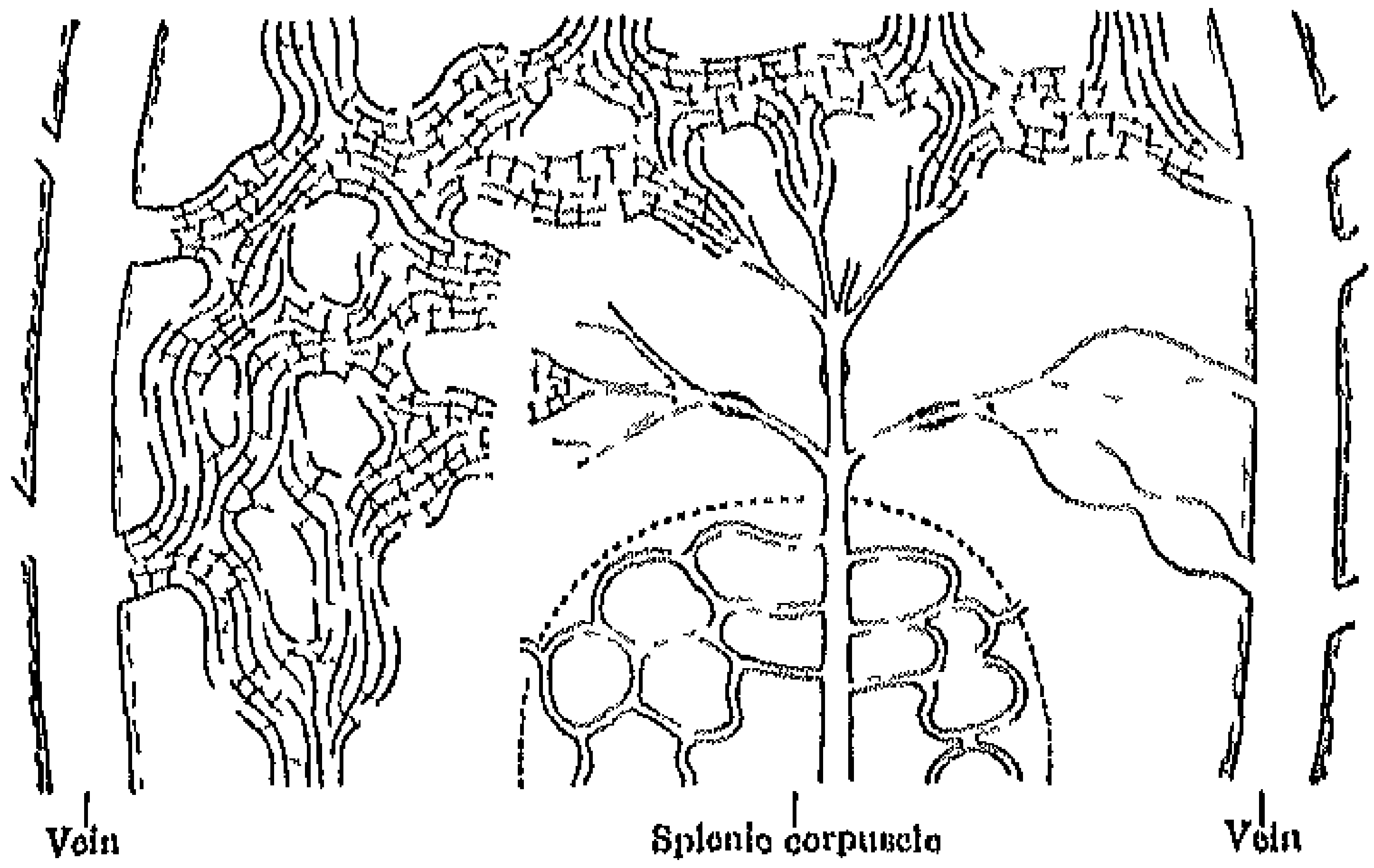


FIG. 106. Diagram to illustrate the theories of circulation in the spleen. Looped capillaries are shown in the splenic corpuscle. The left branch illustrates the "open" type of circulation with fenestrated end bulb; the center branch is partly "closed" but shows pervious sinuses; the right branch is "closed" with impervious sinuses (under normal conditions). Trabecular veins drain the sinuses. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

arterial capillaries) which communicate with the sinusoidal capillaries in the splenic pulp. There is some disagreement as to the exact nature of these terminations. Some, who consider the vascular system as a "closed system," believe the capillaries are directly continuous with the venous sinuses. Others think that from the capillaries the blood goes free into the substance of the pulp and enters the venous sinuses through slitlike openings in their walls.

These venous sinuses extend throughout the red pulp where they anastomose freely with one another. The cells lining the sinuses (known as *special endothelial cells, lining reticular cells* or *littoral cells*) are long, spindle-shaped cells with bulging nuclei which lie with their long axes parallel to the long axis of the vessel. These cells are fixed macrophages rather than the usual typical endothelium and are phagocytic. They are to be considered as part of the reticulo-endothelial system. Some investigators believe these cells are separated by slitlike spaces, which are open when the vessel is expanded and closed when it is contracted, thus allowing cells to enter or leave the blood stream by passing through the wall of the sinusoid by way of these slits. However, such permanent slits have not been demonstrated. Outside of the cells lining the sinuses is a layer of circularly arranged reticular fibers which are continuous with the reticular fibers of the splenic cords.

Knisely, who has studied the circulation in transilluminated spleens, believes that it is a closed system. He found that some of the branches of the sheathed arteries extend without enlargement, to the collecting veins. Others, which constitute the greater number, end in sausage-shaped, pulsating structures, several of which may communicate with one another before joining the vein. Owing to some weakness of constriction, fissures appear in the walls of these enlarged vessels through which blood "leaks" into the pulp. In this manner, cells from the blood stream may enter the pulp, and likewise, may pass from the pulp into the blood stream.

The venous sinusoids join to form the pulp veins, these in turn join to form the trabecular veins, and the splenic vein is formed by the union of the trabecular veins.

The types of cells found in the spleen are: (1) Two kinds of cells forming the reticulum: the undifferentiated cells and the phagocytic reticular cells (fixed histiocytes); (2) Lymphocytes (large, medium and small); (3) Monocytes; (4) Red blood corpuscles; (5) Granular leucocytes; and (6) Megakaryocytes.

The spleen does not possess any afferent lymph vessels as we find in the lymph glands. The lymph vessels which are present are efferent vessels and are found only in the trabeculae and the capsule. There are no lymph vessels present in the parenchyma of the gland.

Nerves to the spleen are nonmyelinated fibers from the sympathetic system. They enter at the hilum and are distributed to the walls of the blood vessels and to the smooth muscle fibers in the capsule and trabeculae. A few myelinated fibers, which are regarded as sensory, have also been observed.

The function of the spleen cannot be considered as vital in the sense that man cannot live without it. It can be removed without any obvious effect; however, its functions are varied and are of importance.

In the foetus the spleen is one site of blood-cell formation. After birth, however, only lymphocytes and monocytes are normally produced there. In certain pathological conditions, nevertheless, the spleen can again assume its full hemopoietic function and produce all types of blood cells.

The spleen is also important in the metabolism of iron in the body. The phagocytic cells of the spleen destroy red blood cells, and iron is salvaged from their hemoglobin. This iron is stored until it is needed for the formation of more hemoglobin.

The spleen also stores large numbers of red blood cells (it can store up to 1/6 of the total red blood cells) and when these cells are needed in the peripheral circulation the spleen contracts by means of the muscle fibers in the capsule and the cells are expelled into the peripheral vessels.

It filters the blood, its phagocytic cells removing any foreign particles, degenerating blood cells, or bacteria. As part of the reticulo-endothelial system the spleen is also thought to be important in the production of antibodies.

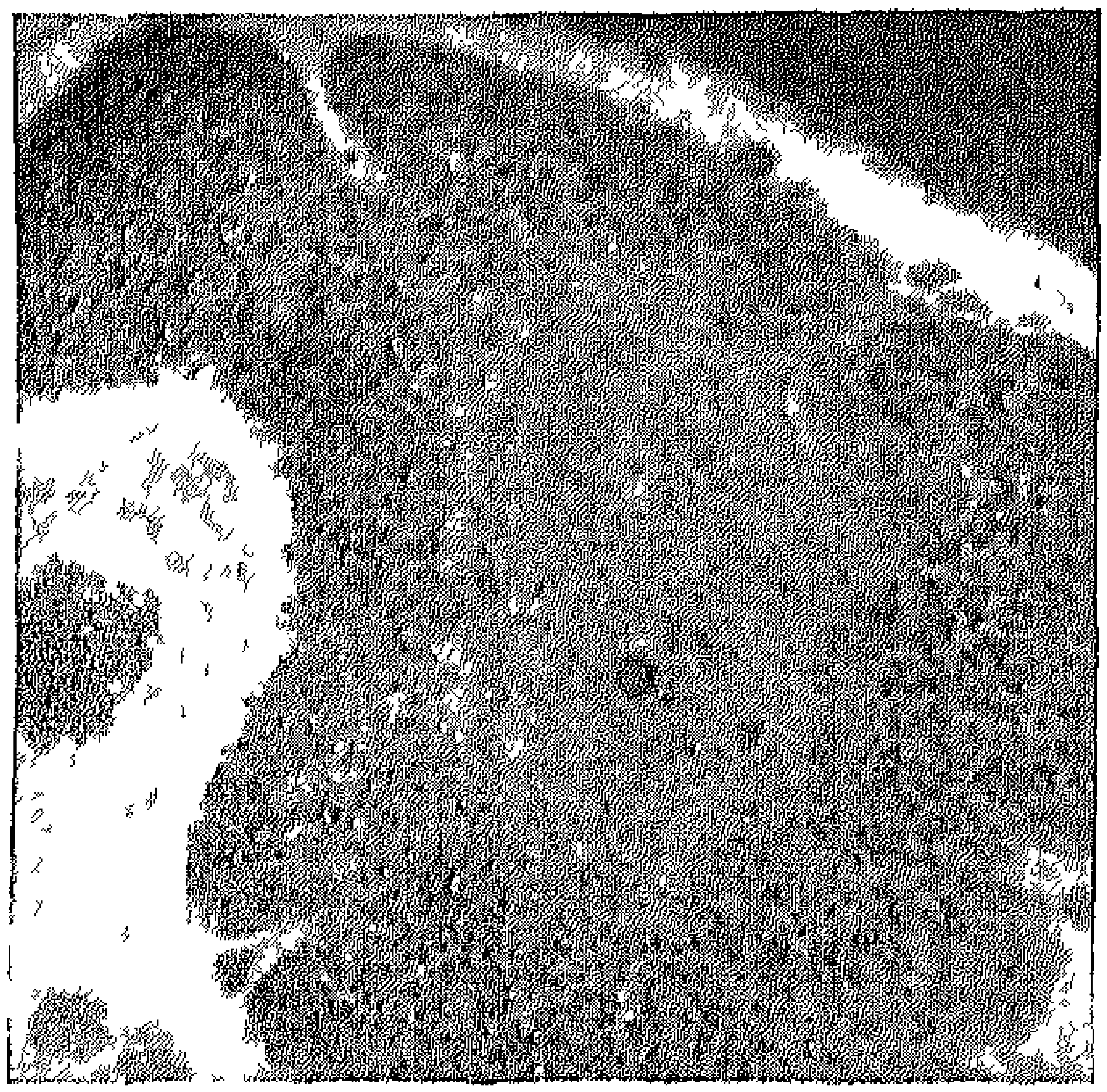


FIG. 107. Section through part of a thymus of a child at birth. Hematoxylin and eosin stain. Photomicrograph.

THE THYMUS

The thymus develops as tubular diverticula from the epithelium of the third pharyngeal pouches. Some people believe that contributions from the cervical sinus are also involved in forming the thymus. These diverticula at first possess a lumen but this disappears as their growth continues downward, the tubelike structures becoming cordlike masses of epithelial cells. The epithelial cells continue to grow and form lateral outgrowths from the cords, which lay the foundations for the later lobulation of the thymus. The cells of the cords undergo a transformation and become stellate in form. The processes of these cells anastomose and establish a reticulum which serves as a framework for the gland. Thymocytes also appear about this same time. As a result of the growth and proliferation of the stellate cells, the lobation of the thymus is more definitely established and its division into a cortex and medulla becomes apparent. There seems to be little question about the origin of the stellate cells of the reticulum from the epithelioid cords. However, there is considerable difference of opinion concerning the origin of the thymocytes. One view is that these cells are epithelial in origin, being derived by proliferation from the cord cells, their resemblance to lymphocytes being fortuitous. Another view, and one that is widely held, is that the thymocytes are true lymphocytes which have migrated into the thymus from the surrounding mesodermal tissue. The absence of nodular formation in the cortex of the thymus has been urged against the lymphocyte origin of these cells. Furthermore, experiments with x-rays undertaken to prove their lymphoid origin have given quite contradictory results. Therefore, the question regarding the true character of these cells is, at present, far from established.

The thymus consists of two elongated, somewhat flattened, lobes which extend from the root of the neck into the upper part of the thorax where they are located behind the sternum. The gland is inclosed by a fibroelastic capsule, extensions of which penetrate its substance and divide its lobes into a number of incompletely formed primary and secondary lobules. These lobules have a peripheral *cortical* area and a central core, the *medulla.*

The cortex is the dense outer portion of the lobules. It consists of the stellate reticulum and numerous small cells closely resembling lymphocytes, which fill the meshes of the stroma. These cells are known as *thymocytes.*

The medulla is considerably lighter than the cortex. It consists of stellate reticular cells and a relatively small number of thymocytes, to which may be added leucocytes, an occasional multinucleated giant cell and a few macrophages. Infrequently in man, but quite constantly in some of the lower animals, a cystlike structure lined with ciliated cells, may be present in the thymus. This probably represents the remains of the tubular diverticulum from the pharyngeal pouches.

The most characteristic structures of the thymus are the *thymic corpuscles (Hassall's corpuscles).* They occur only in the medulla and appear as light areas which are to be recognized by the concentric arrangement of the elements of which they are composed. These corpuscles which appear early in foetal life, are at first few in number, but continue to increase up to the period when the involution of the thymus begins. Thus both small and large corpuscles are present in the medulla at the same time.

A thymic corpuscle results from the growth and transformation of stellate reticular cells. The cell enlarges and as it increases in size, its cytoplasm undergoes certain degenerative changes and becomes filled with a hyaline substance. By its enlargement the cell comes into contact with other cells which are also undergoing similar changes, and which become transformed through pressure, into flattened, crescentic elements concentrically arranged about the central cell. The cells at the center of the corpuscle break down into a formless mass and may even undergo calcification.

A small Hassall's corpuscle may consist of only a single cell which has undergone degenerative changes. These changes are evident in the staining reaction of the nucleus and the development of the hyaline substance in the cytoplasm. The larger corpuscles consist of a central, hyaline mass surrounded by cells which have undergone considerable degeneration and have become concentrically arranged around the central mass.

The branches of the blood vessels which supply the thymus, are located in the connective tissue septa. Capillaries from these vessels pass into the cortex and medulla, the vascular supply of the former being somewhat greater than that of the latter. The larger veins arise in the medulla and leave the thymus by following the course of the arteries.

The lymph vessels which arise in the medulla, and are principally located in the interlobular connective tissue, pass to the neighboring lymph nodes.

Fibers from the thoracic sympathetics and from the vagus nerve end in the walls of the blood vessels and in the medulla.

The thymus grows rapidly from early foetal life until the second year after birth, from which time until puberty its rate of growth is much slower. After puberty the thymus undergoes a process of involution (age involution) in which the thymic tissue is greatly reduced and replaced by fat. In older people the thymus is simply a mass of fat which preserves to some extent, the size and shape of the gland. It contains, however, small patches of thymic tissue which never wholly disappear

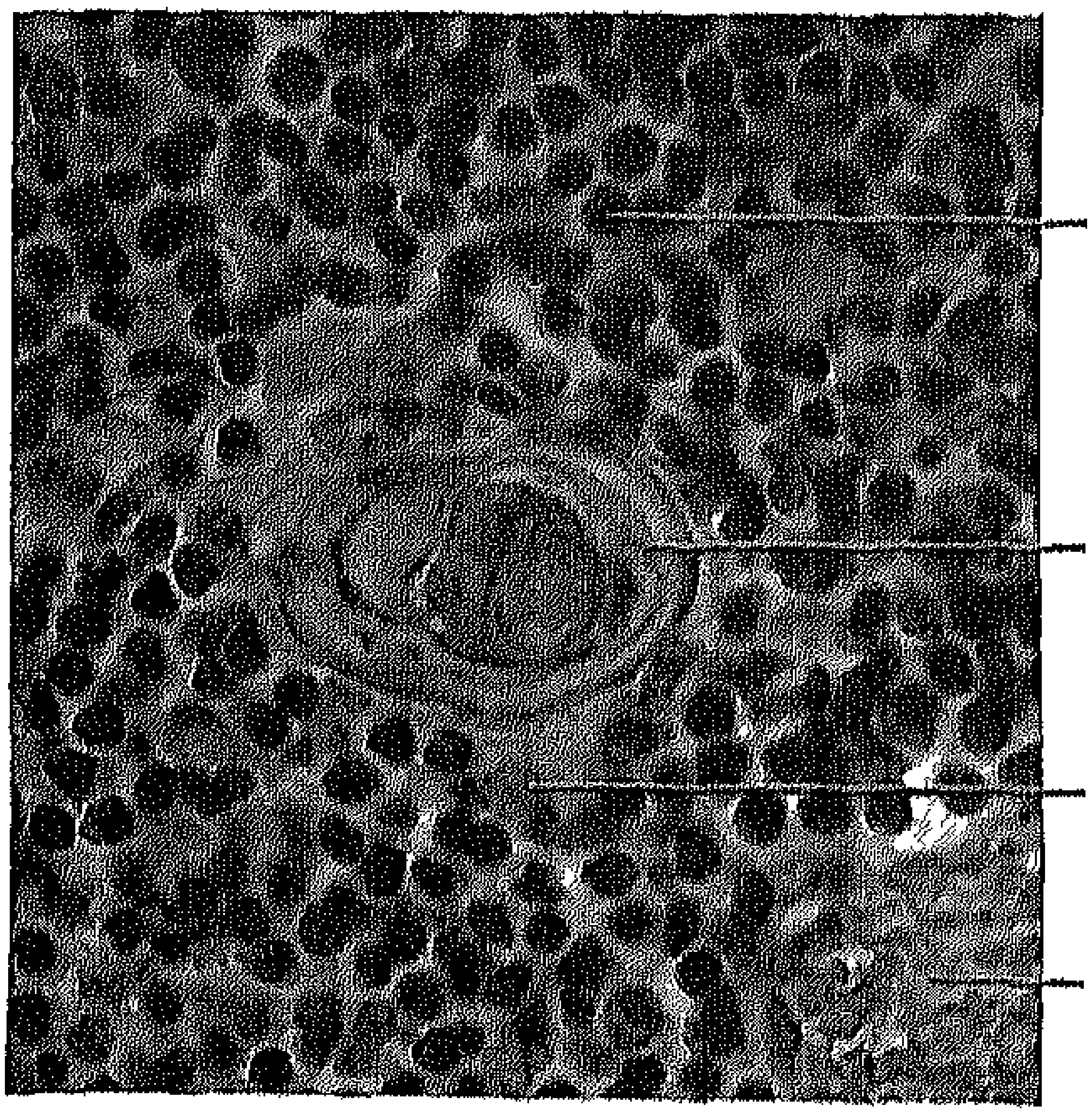


FIG. 108. Medulla of thymus showing a Hassall's corpuscle. Photomicrograph.

from the thymus, even in old age it is present in small amounts. The thymus may show severe atrophy (accidental involution) at any age, but particularly before puberty, as a result of severe infections or wasting diseases.

Although its growth and retrogression is correlated with the process of sexual maturity, in the absence of accidental involution, the exact function of the thymus is not clear. There appears to be an interaction between it and some of the other ductless glands such as the thyroid, adrenals and gonads, since involution of the thymus occurs in the presence of the hormones produced by these glands. Its possible function as an organ of lymphocyte production, although strongly emphasized by some, appears on the whole to be problematical. It is an interesting clinical fact that removal of the thymus in myasthenia gravis relieves the symptoms, but the explanation of why it is effective is unknown.

THE TONSILS

The tonsils are masses of lymphoid tissue located about the passages which lead from the oral and nasal cavities to the pharynx. They are the *palatine* or *faucial tonsils,* the *lingual tonsils,* and the *pharyngeal tonsils (adenoids).* Small accumulations of lymphoid tissue about the openings of the Eustachian tubes into the pharynx are sometimes referred to as the *tubal tonsils.*

THE PALATINE (FAUCIAL) TONSILS. The palatine tonsils are almond-shaped bodies *(amygdalae),* consisting of masses of lymphoid tissue, which are located on either side of the passage (fauces) leading from the oral cavity to the pharynx. They are covered by a thick layer of stratified squamous epithelium. Beneath the epithelium is a layer of reticular tissue *(tunica propria)* which has attained an exceptional depth in this region. The collagenous and elastic fibers of the submucosa are condensed to form a capsular structure which invests the tonsil on all sides, except where it is covered by the epithelium. The reticular tissue is filled with lymphocytes, and together they form a mass of lymphoid tissue within the investing capsule. In sections, striated muscle fibers belonging to the pharyngeal muscle may be seen external to the capsular tissue. The collagenous fibers form a relatively thin, intervening layer between the lymphoid tissue and the muscle. Trabeculae enter the substance of the tonsil from the capsule, and provide not only a pathway for the blood vessels by which the tonsil is supplied, but also form an additional support for the reticular tissue which constitutes its framework.

Each tonsil has 15–20 pitlike invaginations of its epithelium, the *tonsillar crypts.* The epithelium is considerably reduced, and quite thin in the deeper portions of the crypts.

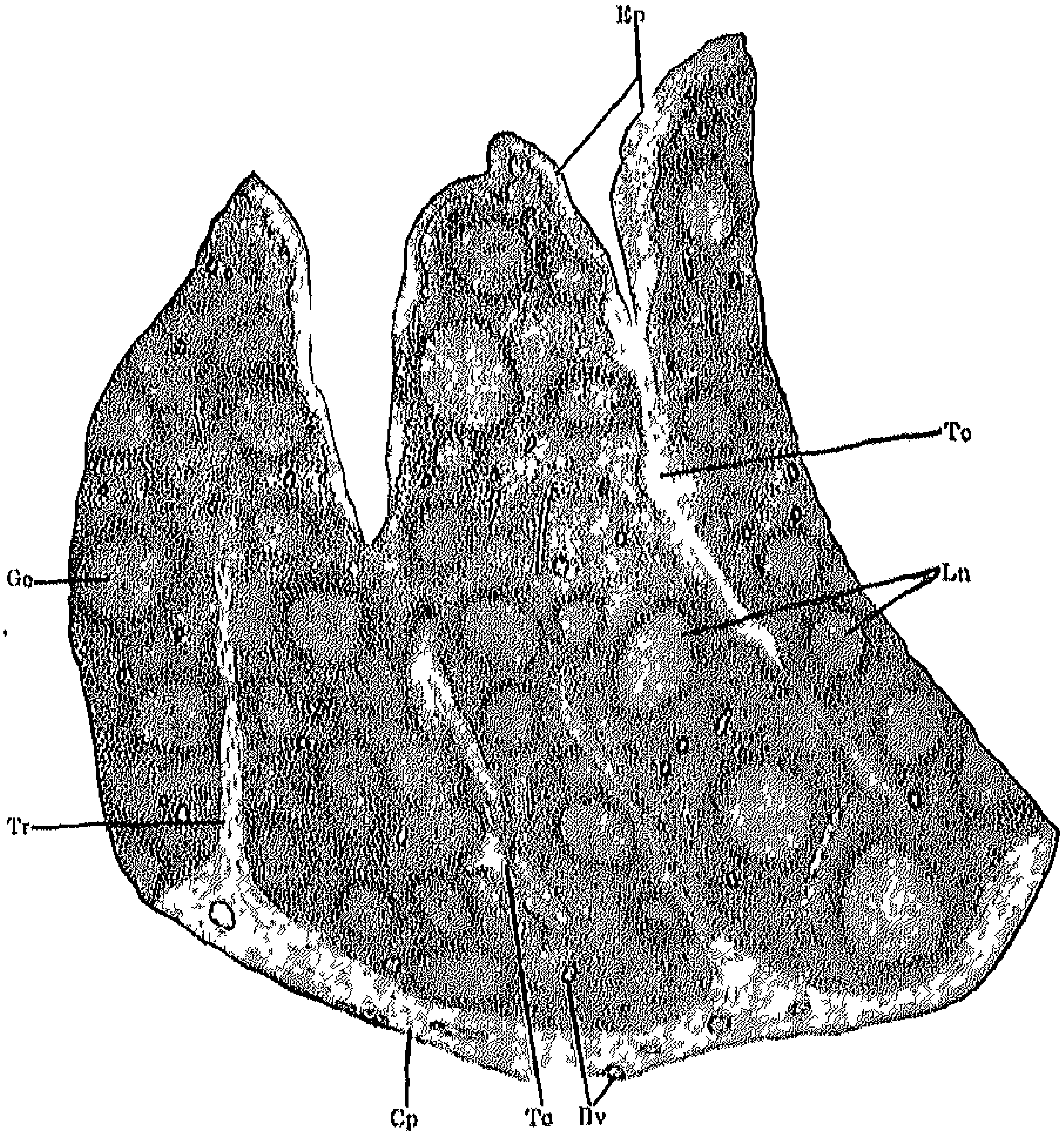


FIG. 109. Section through a faucial tonsil. (Ep) Stratified squamous epithelium covering the tonsil. (Tc) Tonsilar crypt. (Ln) Lymph nodules. (Gc) Germinal center of a nodule. (Cp) Connective tissue capsule. (Tr) Trabecula of connective tissue extending from the capsule into the substance (parenchyma) of the tonsil. (Bv) Blood vessels.

The lymphoid tissue is in the form of nodules, of which there are a considerable number beneath the epithelium and about the crypts. The spaces between the nodules are filled with diffuse lymphoid tissue. Germinal centers are present in some of the nodules and contain small, medium-sized, and large lymphocytes. Mitotic figures in the medium-sized and large cells indicate that the germinal centers are areas of extensive lymphocyte proliferation.

Lymphocytes leave the nodules and enter the diffuse tissue. Some of these cells may enter the blood stream and be carried away from the gland, while others migrate through the epithelium of the crypts and also through the epithelium which covers the surface of the tonsil.

After passing through the epithelium they enter the saliva where they are known as *salivary corpuscles.* The number of lymphocytes invading the epithelium of the tonsil may be so numerous that the epithelial cells in the areas where the invasion is taking place cannot be discerned. However, the epithelium is not destroyed, its cells are merely pushed to one side and flattened. After the passage of the lymphocytes, the epithelial cells resume their normal form and position in the tissue.

Other cells, such as granulocytes, mast cells, and plasma cells may be found intermingling with the cells in the tonsil. Small groups of mucus-secreting glands occur in the connective tissue outside the capsule. The ducts of these glands lead to the surface but, in a few instances, may open into the deep portion of the crypts.

THE LINGUAL TONSILS. The lingual tonsils are located beneath the epithelium which covers the base of the tongue; the accumulations of lymphoid tissue forming rounded elevations on its surface.

The crypts are pitlike invaginations of the epithelium, some of which are branched. They open to the surface, or onto the *foramen caecum,* which is located just behind the circumvallate papillae.

The nodules are clustered around the crypts, the intervening spaces being filled with diffuse lymphoid tissue. Germinal centers are generally present in the nodules. The surrounding connective tissue does not form a definite capsule, but blends with the supporting tissue of the tongue. Mucus-secreting glands are present in the peritonsillar tissue, their ducts leading into the tonsillar crypts.

THE PHARYNGEAL TONSILS. The pharyngeal tonsils are masses of lymphoid tissue located in the posterior wall of the nasopharynx between the pharyngeal openings of the Eustachian tubes. Owing to the thinness of the tissue which lines the roof of the pharynx, the lymphoid tissue in this region is not very thick.

The crypts about which the nodules are gathered are branches from a single large pit which opens to the surface. As in the other tonsils, the nodules are surrounded by diffuse lymphoid tissue.

The epithelium by which the pharyngeal tonsils are covered is of the pseudo-stratified columnar type. When affected by inflammatory conditions, or as age advances, this may change to stratified squamous epithelium. However, the pseudo-stratified epithelium remains unchanged in the bottom of the crypts. In the young, the pharyngeal tonsils are frequently hypertrophied and form large aggregations of lymphoid tissue known as *adenoids.* As age advances, tonsillar tissue may undergo retrogressive changes, and the amount of lymphoid tissue becomes greatly reduced.

The tonsils differ structurally from lymph glands in that they have neither afferent lymph vessels nor lymph sinuses. The efferent lymphatic vessels arise from capillaries around the outer surface of the glands.

The blood vessels which supply the tonsils, enter the capsular tissue from below and at various points along the sides. These vessels pass into the tonsil in the trabecular tissue, which they leave to enter the nodules in the manner already described for the lymph glands and spleen.

The nerves are branches from the sympathetic system, and are distributed to the walls of the blood vessels. Some sensory fibers are also present.

The tonsils contribute to the formation of lymphocytes. They also act as filters for foreign particles and bacteria.

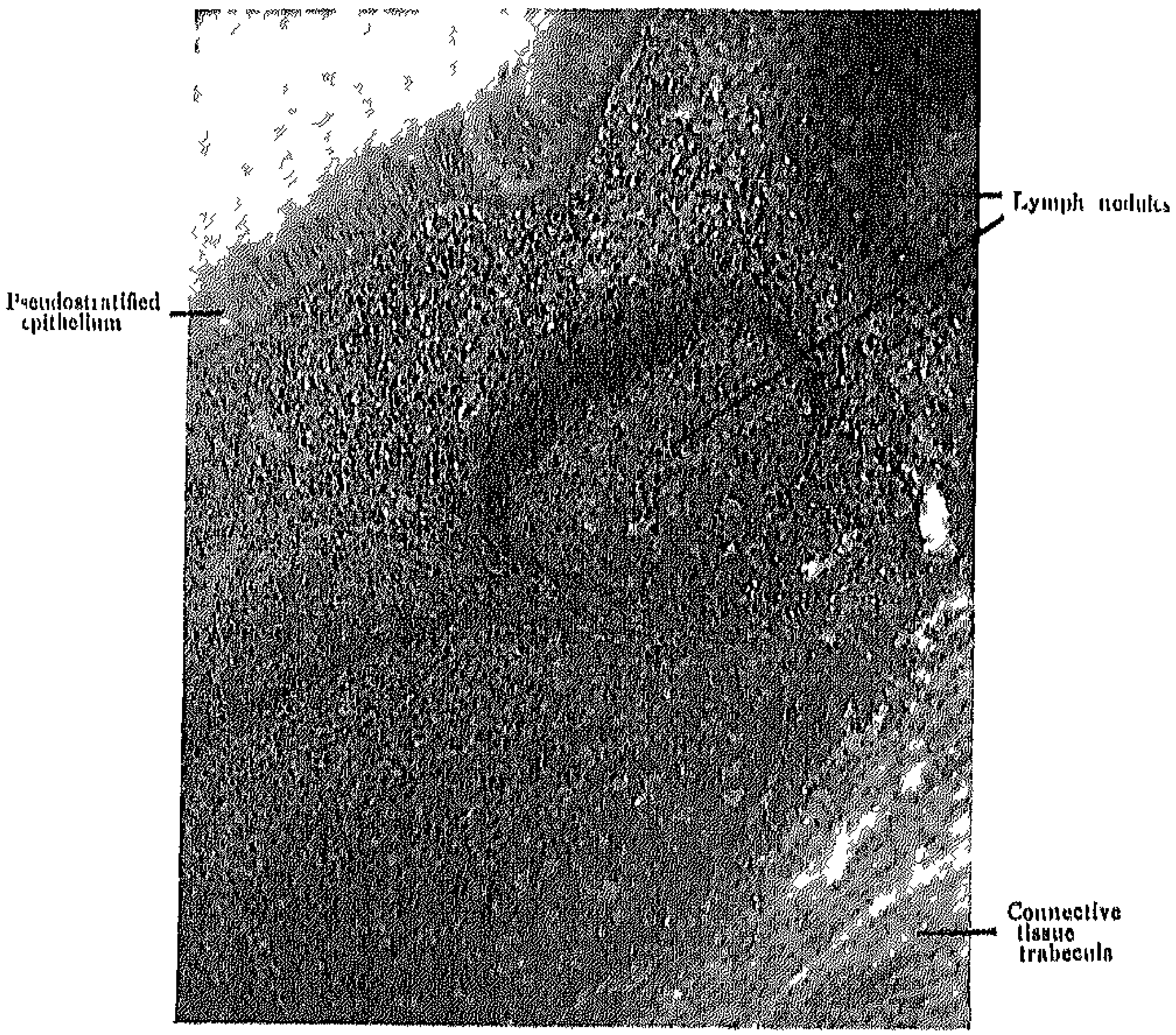


FIG. 110. Section through crypt of a pharyngeal tonsil showing pseudostratified epithelium lining crypt. Photomicrograph.

WALDEYER'S PHARYNGEAL RING

The phagocytic cells produced by the activity of the tonsils, exist for the removal of organisms and particulate matter which lodge on the mucous membrane of the fauces, the oral cavity, and the upper respiratory passages. Therefore, the tonsils are to be regarded as important protective structures. This is also indicated by their arrangement which forms an incomplete ring about the respiratory and oral openings. This ring consists of the pharyngeal tonsils above, the palatine tonsils on either side, and the lingual tonsils below, and is known as the *pharyngeal lymphoid ring of Waldeyer.*

The structure of the lymphoid organs is summarized in the tables which appear on pages 208 and 209.

LYMPHOID ORGANS

Organ	*Capsule*	*Trabeculae*	*Arrangement of Parenchyma*
Lymph glands	Present, well developed	Present, penetrate cortex at right angles to capsule	Lymph nodules in cortex surrounded by diffuse lymph tissue In medulla lymph tissue arranged in branching and anastomosing cords Parenchyma is separated from capsule and trabeculae by lymph sinus
Spleen	Present, relatively thinner than in lymph gland Contains smooth muscle	Present, appear as incomplete partitions Contain smooth muscle	Lymph nodules in relation to central artery
Tonsils:	Present, but only on embedded surface	Present	Lymph nodules and diffuse lymphoid tissue
Pharyngeal	Poorly defined	Present	Lymph nodules are clustered about crypts Remainder is diffuse lymphoid tissue
Palatine	Well defined	Present	Lymph nodules beneath epithelium and around crypts Remainder is diffuse lymphoid tissue
Lingual	Not definite. It blends with connective *tissue of the tongue*	None	Lymph nodules are clustered about crypts *Remainder is diffuse lymphoid tissue*
Thymus	Present	Interlobular septa, no intralobular trabeculae	Dense layer of diffuse lymphoid tissue (thymocytes) in cortex Less diffuse lymph tissue (thymocytes) in medulla

NOTE: The stroma of all lymphoid organs is formed by reticular tissue, supported by connective tissue septa or trabeculae and, in some organs, enclosed by limiting capsule. The parenchyma is formed of lymphoid tissue (thymocytes in thymus).

LYMPHOID ORGANS

Organ	*Cortex*	*Medulla*	*Characteristic Structures*	*Epithelium*
Lymph glands	Present	Present	Capsule Lymph sinus Trabeculae Nodules in cortex Cortex and medulla	None
Spleen	Absent	Absent	Capsule (with smooth muscle) Incomplete trabeculae Lymph nodules with central artery White pulp (dense lymphoid tissue) Red pulp (contains numerous red blood corpuscles)	None
Tonsils:	Absent	Absent	Partial capsule Epithelium Crypts Lymph nodules	Present
Pharyngeal				Pseudostratified
Palatine				Stratified squamous
Lingual				Stratified squamous
Thymus	Present	Present	Thin capsule Lobules Cortex (dense peripheral layer) Medulla (lighter staining central portion) Hassall's corpuscles Thymocytes forming parenchyma	None

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The Digestive System

The digestive system consists of the *alimentary tract* and *accessory glandular organs*. The function of this system is to reduce food materials to a condition which will permit their absorption into the blood stream, and the removal of residual waste material from the body. The process by which these functions are accomplished is partly mechanical and partly chemical. The various digestive organs are structurally adapted to the parts of the process they have to perform.

The digestive tube consists of the *mouth*, *pharynx*, *esophagus*, *stomach*, *small* and *large intestines*, *rectum* and *anal canal*. From the mouth to the stomach, with the exception of a short portion of the esophagus which lies below the diaphragm, the tubular portion of the alimentary tract is surrounded and supported by connective tissue. In the abdominal cavity the greater portion of the intestines hangs free yet is attached to the body wall by folds of mesothelium supported by connective tissue. These folds form the mesenteries and are a continuation of the *peritoneum* by which the abdominal cavity is lined.

Structurally the mouth and pharynx differ from the other portions of the alimentary tract. The mouth is adapted by special structures, the teeth and tongue, to the mechanical process of mastication, whereby the food is reduced to small masses and mixed with the secretion of the salivary glands in preparation for swallowing. The structure of the pharynx is adapted to enable it to perform a double function of serving both the digestive and respiratory systems. The chemical work of digestion, and the processes of absorption, take place in the stomach and intestines, the epithelium which forms their lining being modified to meet these requirements. Their walls also contain numerous glands which produce substances that are active in the process of digestion, or by which the passage of food through the tube is facilitated. The lower portion of the tract is less concerned with digestion and absorption than with the passage of the unused residue, hence its structure is adapted to the work of elimination.

In spite of special structural modifications in various areas of the digestive tract from the beginning of the esophagus through the rectum, which occur in response to the functional demands of particular regions, there is a fundamental structural plan for the entire tract on which these specialized structures are imposed. This common structural plan consists of a tubular structure whose wall is made up of five layers: (1) A *mucosa,* which lines the lumen of the tube and consists of an epithelium resting on a layer of reticular tissue called the *tunica propria (membrana propria).* (2) A *muscularis mucosae,* which is a thin layer of smooth muscle fibers that lies between the tunica propria and the subjacent tissue. Since the muscularis mucosae is associated with the mucosa only in the digestive tract it will be considered as a separate entity, which in this particular location is interposed between the mucosa and the underlying submucosa. (3) The *submucosa* is a loosely arranged layer of collagenous and elastic fibers which gives support to blood vessels, lymphatics and nerves. (4) Encircling the submucosa is a coat of smooth muscle, the *muscularis externa,* consisting of an inner layer that is circularly arranged and an outer layer that is longitudinally arranged. (5) In the esophageal and rectal segments, the outermost layer, the *adventitia,* consists of fibrous connective tissue, by means of which these portions of the tube are firmly attached to the adjacent structures. Throughout the remaining extent of the tube the outer investment is called the *serosa* or *serous coat* (loose connective tissue covered by a single layer of mesothelium) and consists of that part of the mesentery by which the greater part of the abdominal portion of the alimentary canal is invested.

Throughout the length of the alimentary canal there is little variation in the form and arrangement of the submucous and muscular coats. The parts which are almost completely enveloped by a serous coat are the portion of the esophagus that lies below the diaphragm, the stomach, the greater part of the small intestine, and that part of the large intestine known as the transverse colon. The remainder of the large intestine is covered by a serous membrane on one of its surfaces; the surface which does not have a serous coat is attached to the body wall by connective tissue. The rectum is enclosed by an adventitia, as is the esophagus above the diaphragm.

THE LIPS

The upper and lower lips bound the aperture *(rima oris)* which leads into the mouth. Each lip presents an external or *cutaneous* surface and an oral or *mucous* surface. The *border* of the lip lies between the two surfaces, from which it is separared by poorly defined anterior and posterior angles. It varies in thickness in different individuals.

The cutaneous surface is covered by an integument consisting of a stratified squamous epithelium, the *epidermis,* which rests on a dense layer of fibroelastic tissue, the *corium* or *derma*. Together, the epidermis and corium form the skin. The epidermis is extremely thin, its external layer consisting of hard, cornified cells. The papillae are low and not especially numerous. The collagenous and elastic fibers which form the subcutaneous tissue *(tela subcutanea)* beneath the corium are loosely arranged and contain small masses of fat cells.

The structures associated with the integument are the *hair follicles, sebaceous glands* and *sweat glands*. The hair follicles are tubular invaginations of the epidermis which extend deeply into the corium. In sections, portions of the hair shaft are frequently observed in the follicles. The sebaceous glands, which are associated with the hair follicles, are saclike structures filled with relatively large, polyhedral cells. The yellowish color of these glands is due to the oily nature of their secretion. The sweat glands are long, slender epithelial tubes which extend from the surface of the epidermis into the deep portions of the corium, their coiled secreting portions frequently lying in the subcutaneous tissue. (For details of structure of skin see p. 366.)

The epithelium increases in thickness as it passes over the anterior angle to the border of the lip. It also becomes more deeply papillated. The rich supply of blood capillaries in the papillae, which extend almost to the surface of the epithelium, gives the border its deep red color. The thickened epithelium passes over the posterior angle to continue as the lining of the oral cavity.

Covering the posterior surface of the border of the lips of infants, the epithelium develops an unusual thickness and is characterized by a large number of deep, narrow papillae. This overgrowth *(hypertrophy)* of the tissue is due to pressure stimulus, resulting from the contact of the lips with the nipple, and is known as the sucking disc.

The mucous membrane, which lines the inner or oral surface of the lip, consists of a stratified squamous epithelium resting on a thin *tunica propria*, beneath which is a layer of loosely arranged fibroelastic tissue forming a submucosa. The epithelium is considerably thicker than that on the cutaneous surface and is more deeply papillated. The surface cells, owing to their moist environment, are not as extensively cornified. The tunica propria is a thin layer of reticular tissue which is almost invisible with ordinary magnifications, its presence being indicated by a line of scattered lymphocytes. The submucosa contains aggregations of glandular tissue, the *labial glands*, the acini of which are composed of mixed mucus- and serous-secreting cells. Some of the labial glands are deeply placed and lie between the muscle bundles. They belong to the class known as branched tubuloacinar glands (see section on glands). In sections, their ducts can frequently be traced to the surface of the epithelium on which they open.

As seen in section, the mid-portion of the lip is occupied by bundles

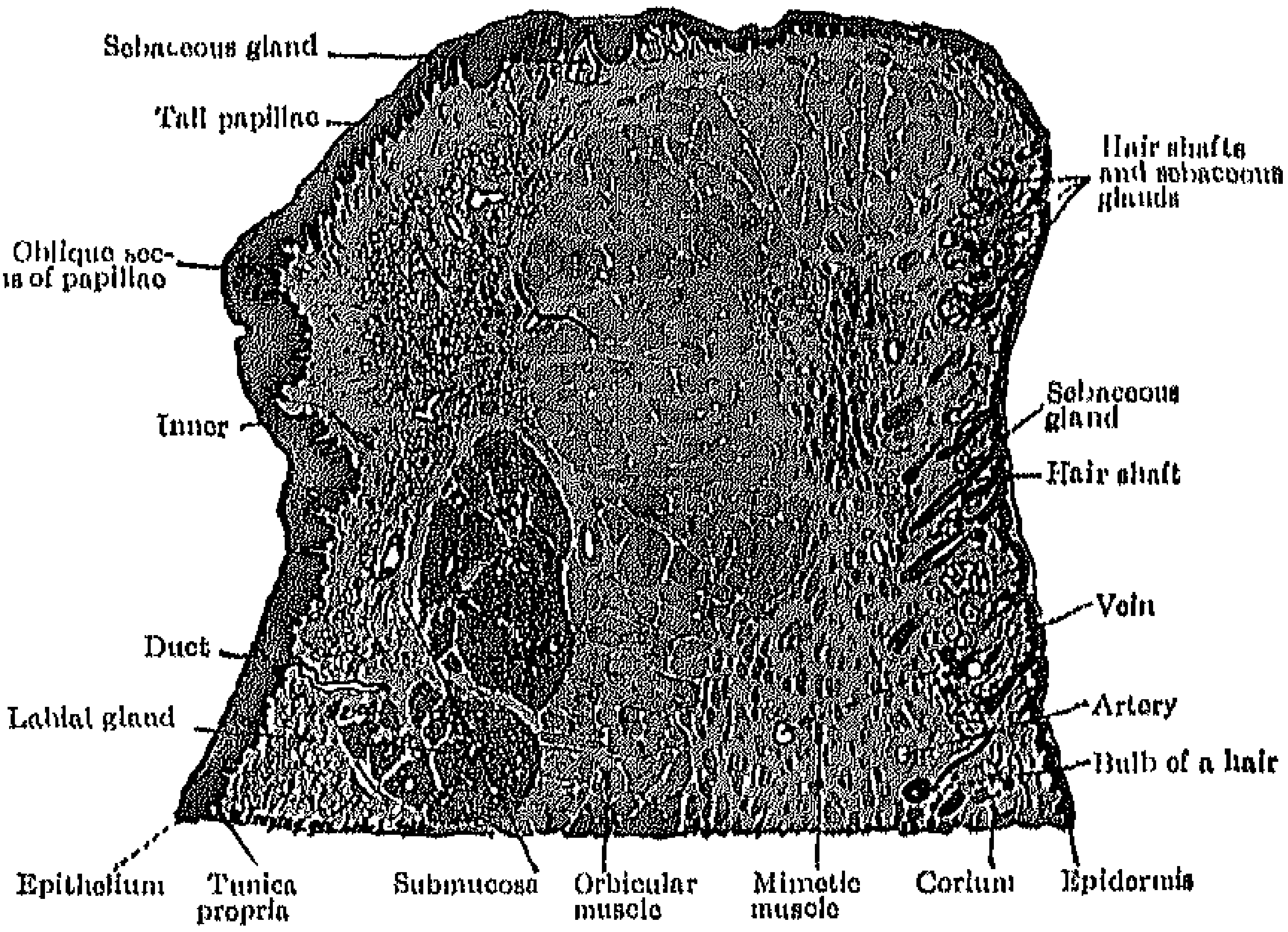


FIG. 111. Vertical section through the lower lip of a man of nineteen years. 10 X. Epidermis and corium constitute the skin; epithelium, t. propria, and submucosa form the oral mucous membrane. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

of striated muscle *(M. obicularis oris)*, the fibers of which are cut transversely. The muscle bundles are separated by septa of connective tissue which extend from the subcutaneous tissue to the submucosa.

The blood supply of the lip is through the labial branches of the external maxillary artery. These branches form a plexus in the subcutaneous and submucous tissue, from which smaller branches pass to the various structures in the lip.

The nerve supply is by both myelinated and unmyelinated fibers. The myelinated fibers are branches of the trigeminal nerve which, after losing their myelin sheaths, end in sensory corpuscles in the papillae or as free fibers among the cells of the epithelium. The unmyelinated fibers are from the autonomic system and end in relation to the walls of the blood vessels, the labial glands, sweat glands and hair follicles.

THE MOUTH

The alimentary canal begins with the mouth which is closed anteriorly by the lips. Posteriorly the oral cavity is continuous with the pharynx. It contains the tongue and the teeth and receives the secretions of the salivary glands. It is lined by a mucous membrane which becomes continuous with the mucous membrane covering the inner surface of the lips. The mucous membrane consists of a layer of stratified squamous epithelium which rests on a connective tissue stroma. Owing to their moist environment, the surface cells of the epithelium are not extensively cornified. The superficial cells are readily desquamated and appear in the saliva as flattened epithelial elements. The epithelium is penetrated by papillae from the underlying connective tissue. The papillae are best developed and are most numerous in those portions of the mucous membrane which are most highly sensitive.

There is no muscularis mucosae.

Underlying the mucous membrane is a submucous layer consisting of collagenous tissue and a few elastic fibers which give support to blood vessels, lymphatics and nerves. There is no submucosa beneath the epithelium of the hard palate, the connective tissue of the mucous membrane consisting of a thin layer of fibers which merges with the periosteum of the bone. There is considerable variation in these layers in the various parts of the mouth, which involve differences in the thickness of the epithelial layer and in compactness of its underlying stroma, the number and height of the papillae, the character and thickness of the submucosa.

Both mucus- and serous-secreting glands are present. They are small branched tubular structures whose secreting portions for the most part extend into the submucosa. Where the submucosa is entirely missing or extremely thin, the glands are few or absent.

The blood vessels form a plexus in the submucosa from which looped capillary branches extend into the papillae.

For the most part, the smaller lymphatic vessels and capillaries are found in the stroma under the epithelium. The larger vessels of this area drain into still larger vessels in the submucosa.

The mucous membrane is supplied with both myelinated and unmyelinated nerve fibers. The myelinated fibers are sensory and end in corpuscles in the papillae, or as free terminal branches in the epithelium. The unmyelinated fibers are from the autonomic system and end in the walls of the blood vessels.

THE TEETH

Due to their extensive calcification, the teeth are the hardest structures in the body. They appear in two sets: the *deciduous teeth (milk dentition),* which begin to erupt about the sixth or seventh month after birth and are shed between the sixth and twelfth year, and the *permanent dentition,* which follows the shedding of the milk dentition and is completed about the eighteenth year or even later.

The varying forms of the teeth are an adaptation to the purposes for which they are used. The *incisors,* with their chisellike edges, are for biting; the fanglike *canines* are employed for tearing; while the *premolars* and *molars*, which have their occlusal surfaces divided by furrows into two or more cusps, are arranged for grinding the food.

The teeth are set in pitlike excavations *(alveoli)* in the bony rim of the jaw. The jaw is covered by a layer of epithelium and subepithelial connective tissue, forming the *gum (gingiva)*. As it approaches the surface of the tooth, the epithelium dips downward, forming a space between the tooth and the gum known as the *gingival crevice*. The

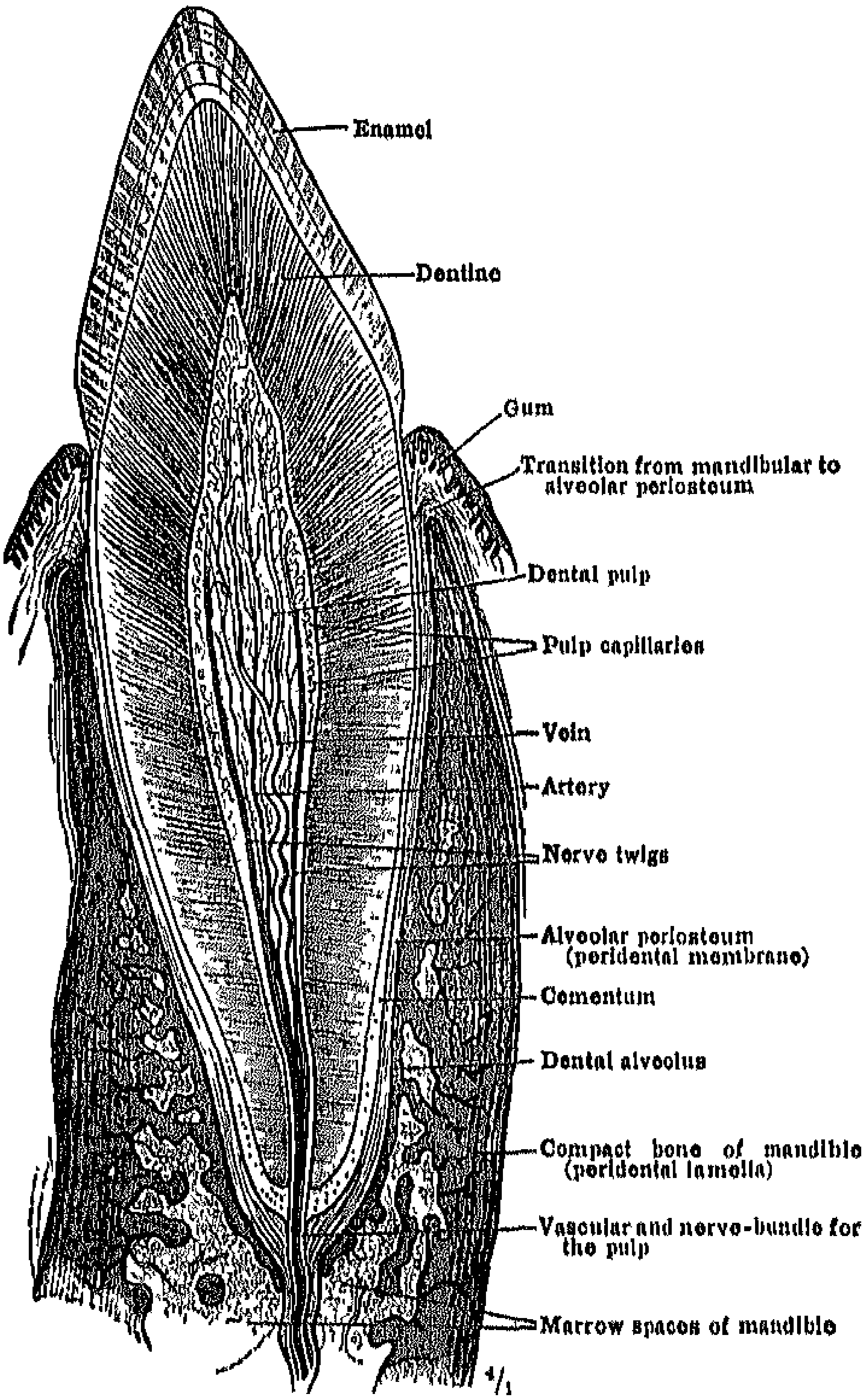

Enamel
Dentine
Gum
Transition from mandibular to alveolar periosteum
Dental pulp
Pulp capillaries
Vein
Artery
Nerve twigs
Alveolar periosteum (peridental membrane)
Cementum
Dental alveolus
Compact bone of mandible (peridental lamella)
Vascular and nerve-bundle for the pulp
Marrow spaces of mandible
4/1

FIG. 112. Vertical section of an inferior canine tooth, in situ. 4 ×. (Toldt.) (Courtesy, J. Parsons Schaeffer, Ed.: "Morris' Human Anatomy," Philadelphia, The Blakiston Company.)

rim of the jaw in which the teeth are set is called the *alveolar border.* The epithelium and connective tissue of the gum are continuous with the mucous membrane of the oral cavity.

The portion of the tooth which extends above the gum is called the *crown.* The *root* is the portion which extends into the alveolus and the *neck* is the slightly constricted part between the root and the crown. The connective tissue of the alveolar border is continued into the alveolus, about the root, and forms the *peridental membrane.*

Although the teeth are similar to bone in respect to hardness, and to some extent in their formation, they do not belong to the skeletal system, but are ectodermal structures which arise from the epithelium that lines the oral cavity.

The teeth are composed of three fundamental dental tissues: *enamel, dentine,* and *cementum.* The enamel, which covers the crown, is the hardest and most resistant. It is thickest on that portion of the crown which comes in contact with the food and with the other teeth, and becomes progressively thinner toward the neck where it ends. The dentine underlies the enamel and cementum. It conforms to the general shape of the tooth and provides the foundation on which the other structures of the tooth are built. The cementum is the external covering of the root. It presents a lamellated structure similar to that of bone (it does not, however, contain Haversian systems), and contains lacunae and canaliculi in which cement cells are arranged in a manner comparable to the osteocytes occupying the lacunae in bone.

THE ENAMEL. While the enamel organ is the first part of the tooth to appear, actually the deposition of enamel and dentine occur almost simultaneously. Enamel is an extremely hard substance consisting of 96 per cent inorganic material, the remaining 4 per cent being organic material and water. It consists of a series of hexagonal, rodlike structures, the *enamel rods, rod sheaths,* and a *cement substance.*

The enamel rods extend obliquely from the dentinoenamel junction to the surface of the tooth. During development each enamel rod is formed by a corresponding enamel cell or *ameloblast.* The rods are laid down in successive layers as a soft, pre-enamel substance which undergoes a rapid calcification. The process by which the substance of the enamel is deposited is not continuous, but consists of alternate periods of activity and rest. During the inactive period the rate of calcification is lessened. Calcification begins near the free surface of each rod and spreads toward the attached end. This spread is not uniform throughout each enamel rod, but the calcification occurs sooner on one side than the other. This accounts for the odd impressions seen in the walls of enamel rods.

The rod sheath is a thin layer at the periphery of the enamel rod that has a somewhat different refractive index than the rest of the enamel. It differs from the enamel rod by containing more organic material and being less completely calcified.

A cement substance binds the enamel rods together. In ground sections it is apparent as a narrow line that is somewhat more refractive than the rod sheaths.

In general the enamel rods lie at right angles to the surface of the underlying dentine. Their length is variable depending on their direction and the thickness of the enamel they traverse. The rods are

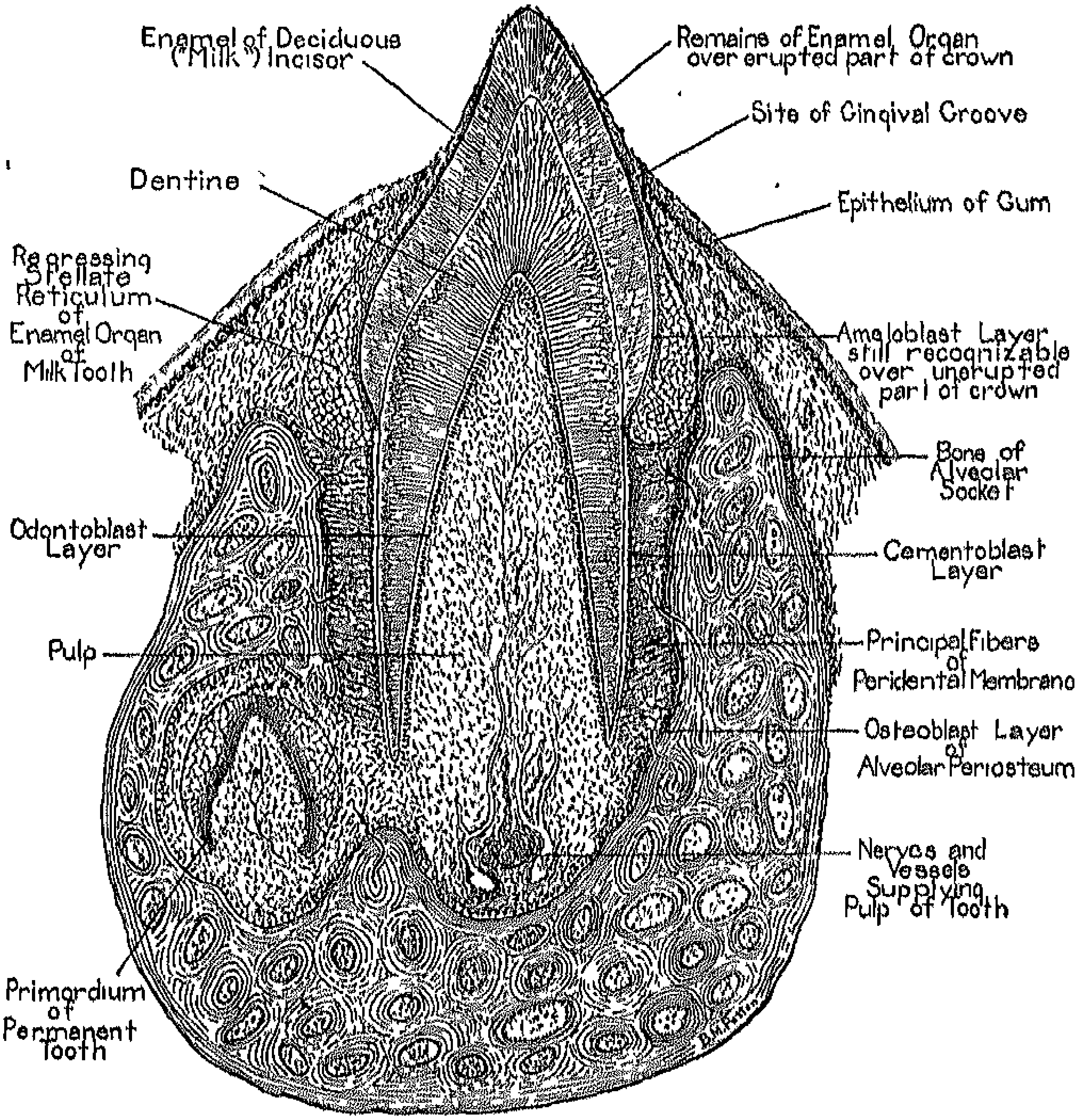

Enamel of Deciduous ("Milk") Incisor
Dentine
Regressing Stellate Reticulum of Enamel Organ of Milk Tooth
Odontoblast Layer
Pulp
Primordium of Permanent Tooth
Remains of Enamel Organ over erupted part of crown
Site of Gingival Groove
Epithelium of Gum
Ameloblast Layer still recognizable over unerupted part of crown
Bone of Alveolar Socket
Cementoblast Layer
Principal Fibers of Peridental Membrane
Osteoblast Layer of Alveolar Periosteum
Nerves and Vessels Supplying Pulp of Tooth

FIG. 118. Diagrammatic representation of a partially erupted milk tooth. The root formation is incomplete, but the arrangement of the tissues around the developing root indicates the method by which it will be attached within the alveolar socket. (Courtesy, Patten: "Human Embryology." Philadelphia, The Blakiston Company.)

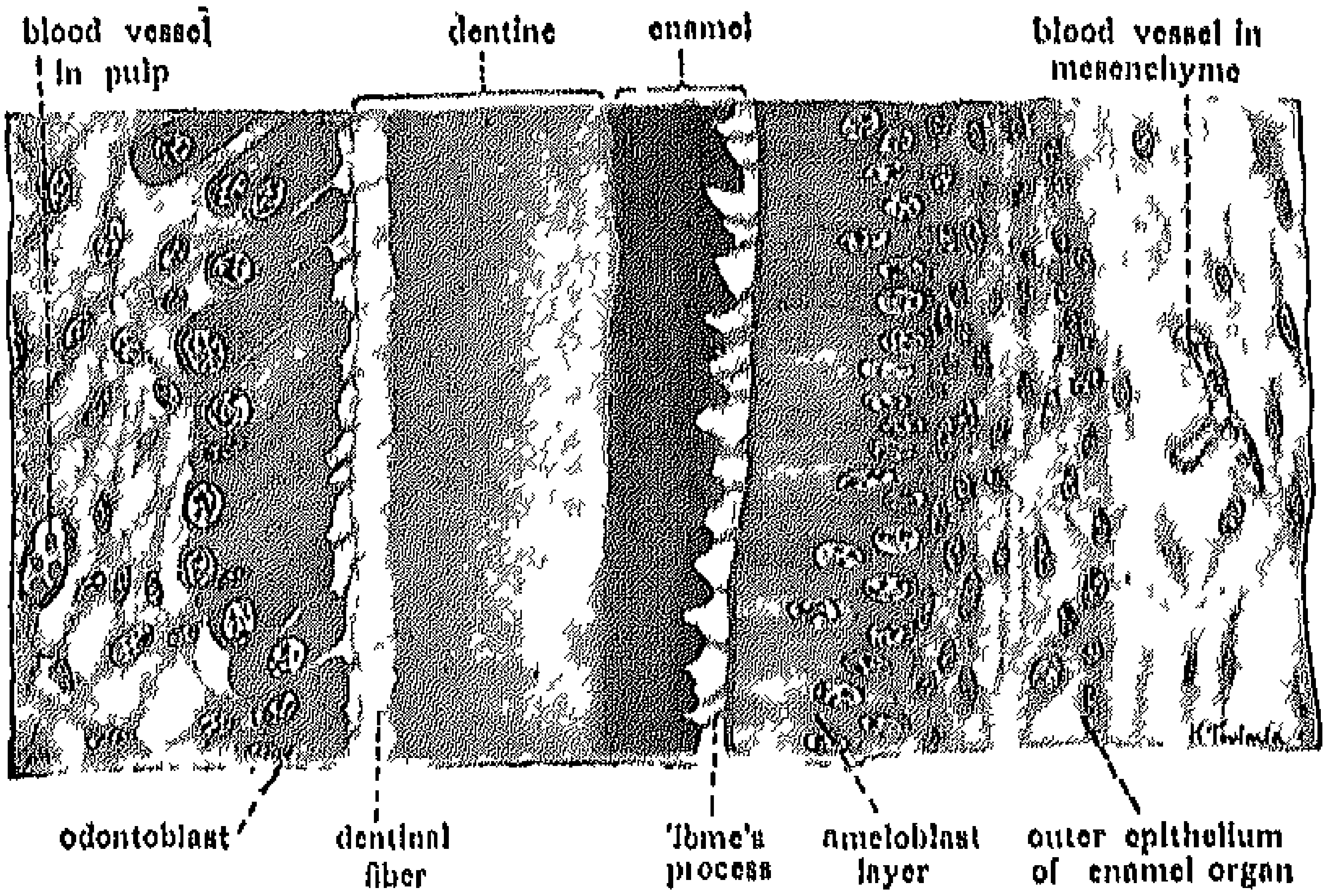


FIG. 114. Projection drawing of small segment of developing incisor from 130 mm. pig embryo to show formation of enamel and dentine 350 ×. (Courtesy, Patten: "Embryology of the Pig," Philadelphia, The Blakiston Company)

not straight tubular structures but show varying degrees of waviness.

In longitudinal sections of ground sections of a tooth, a series of dark lines are seen; they extend over the tip of the dentine and on the sides of the tooth they extend obliquely upward from the dentino-enamel junction to the surface of the tooth. These lines are due to differences in the rate of formation of enamel matrix and are known as the *lines of Retzius* or "incremental" lines. When seen in cross section of a tooth, these lines appear as a series of concentric rings occurring at regular intervals and they have been compared to the growth rings in the cross section of a tree.

The growth of enamel takes place more rapidly over the crown of an incisor or cusp of a molar, than on the sides. This results in an increase in its surface area with a corresponding difference both in the length and in the direction of the enamel rods. When the enamel is observed in ground tooth sections, some of the rods are cut transversely, others obliquely, and still others longitudinally. When such a section is viewed by reflected light, the areas in which the rods are cut transversely appear dark; those which are sectioned obliquely and longitudinally appear light. The section thus presents broad light and dark areas which are due to the direction of the enamel rods. These alternating light and dark areas are known as the *bands of Hunter-Schreger.*

When the tooth erupts it is covered by a thin, structureless membrane called the *enamel cuticle.* This structure gradually disappears as a result of wear due to the effects of various mechanical influences (chewing, etc.).

During the development of the tooth, various lines or imperfections appear in the enamel due to disturbances in the calcification of this layer. The most common of these imperfections are: *enamel lamellae*, *enamel tufts*, and *enamel spindles*.

Enamel lamellae are irregularities or cracks which run the entire width of the enamel. They usually extend in a direction parallel to the long axis of the crown of the tooth, and are produced in developing enamel along lines of tension.

Enamel tufts begin at the dentinoenamel junction and extend for a variable distance into the enamel. Their odd tuftlike appearance is due to the projection into a single plane (effect produced by observing them under low magnification) of groups of curved fibers that actually lie in many different planes. These tufts are poorly calcified enamel rods, together with a good deal of cement substance.

The dentinoenamel junction is not a smooth, uniform line but is irregular, due to spindlelike processes of the odontoblasts (dentine producing cells) which have extended into the enamel layer before it was completely calcified. These processes are known as enamel spindles.

DENTINE. The greater part of the tooth is made up of dentine, which conforms to the general shape of the tooth. In the region of the crown it is covered by the enamel, while in the region of the root the cementum rests upon it. Chemically it is made up of approximately 70 per cent inorganic material and 30 per cent organic matter and water. The calcification of dentine is not so extensive as that of enamel, hence it is somewhat softer and more elastic, a condition which is essential for the support it gives the enamel against applied pressure. Unlike enamel, which is a product of the ectoderm, dentine is derived from the mesoderm. Dentine is similar to bone in its chemical components. Both have a dense, hard matrix, however, they differ in that the bone matrix contains osteocytes and lacunae, while the dentine contains numerous fine tubules, the *dentinal tubules*, in which are found long protoplasmic processes extending from the cells (odontoblasts) that line the pulp cavity. These processes are known as the *dentinal fibers of Tomes*. The substance of the dentine immediately surrounding the tubules is especially resistant to the action of alkalies and acids, and forms the *sheaths of Newmann*. Owing to the fact that the tubules form small spirals in their course through the dentine, they have a wavy appearance in sections. As they approach the dentinoenamel junction they break up into a number of delicate, anastomosing branches. Most of the tubules do not pass into the enamel, although a few may be observed to end in connection with the enamel spindles, or between the enamel rods.

Between the dentinal tubules the matrix consists of a calcified

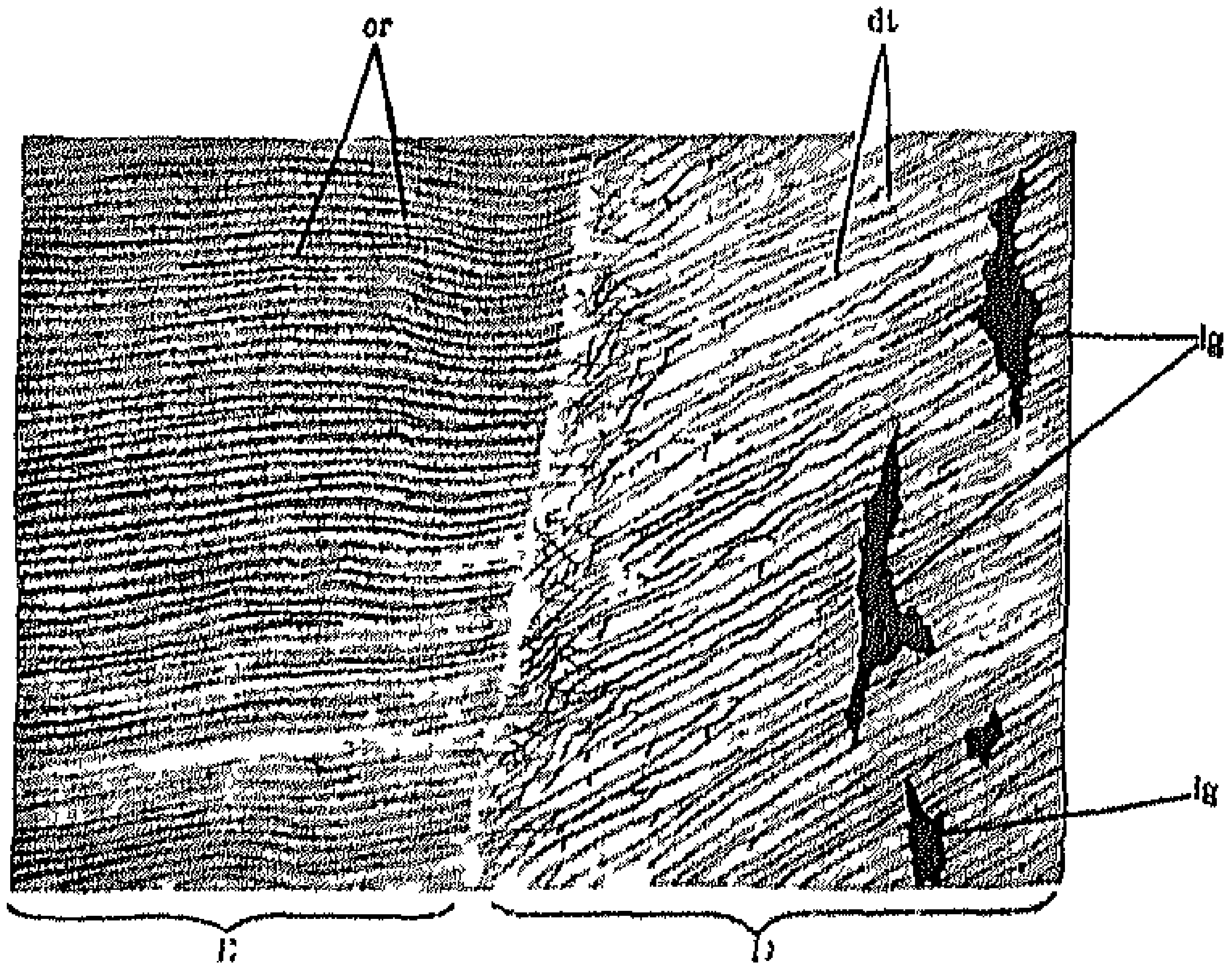


FIG. 115. Junction of the enamel and dentine at the crown of the tooth. (E) Enamel (D) Dentine. (er) Enamel rods. (dt) Dentinal tubules. (ig-ig') Interglobular spaces. (Drawn from Sobotta's Atlas.)

cement substance in which are numerous fine collagenous fibrils. These fibrils are arranged in bundles and, in general, run perpendicular to *the dentinal tubules.*

Areas occur in the dentine in which the organic base fails to calcify, *especially beneath the enamel which covers the crown of the tooth.* When seen in ground sections these areas appear as dark, irregular spaces known as the *interglobular spaces.* Actually they are areas which are poorly calcified and the organic material is replaced with air. Somewhat similar appearing spaces always occur in the dentine immediately adjacent to the cementum which covers the root. These spaces differ from the interglobular spaces only in their location and size. Due to their small size they appear as granules when seen under low magnification and because of this, the area in which they occur has been named the *granular area of Tomes.* These spaces contain organic material which is supposed to be sensitive to thermal and chemical stimuli, in spite of the fact that it has been impossible to demonstrate nerve fibers in these spaces. It is thought that these stimuli may reach the underlying nerve fibers by way of the dentinal fibers and the cell bodies of the odontoblasts. The dentinoenamel junction is also a very sensitive area.

THE CEMENTUM. The cementum is the last of the fundamental dental tissues to be developed, its function being to provide a firm anchorage for the tooth in the jaw. Cementum is a substance not unlike bone in its composition and structure. It is laid down on the dentine of the root in much the same manner in which subperiosteal bone is formed. Connective tissue cells are transformed into *cementoblasts* which deposit the cementum in layers or lamellae. The lamellae are thin in the region of the neck but increase in thickness toward the apex or terminal end of the root of the tooth. The fact that a lamella may be thicker in one part than in another indicates that the rate at which the cementum is deposited varies in different regions. There is also a variation in the character of the cementum which may be almost transparent in one region and dense and granular in another.

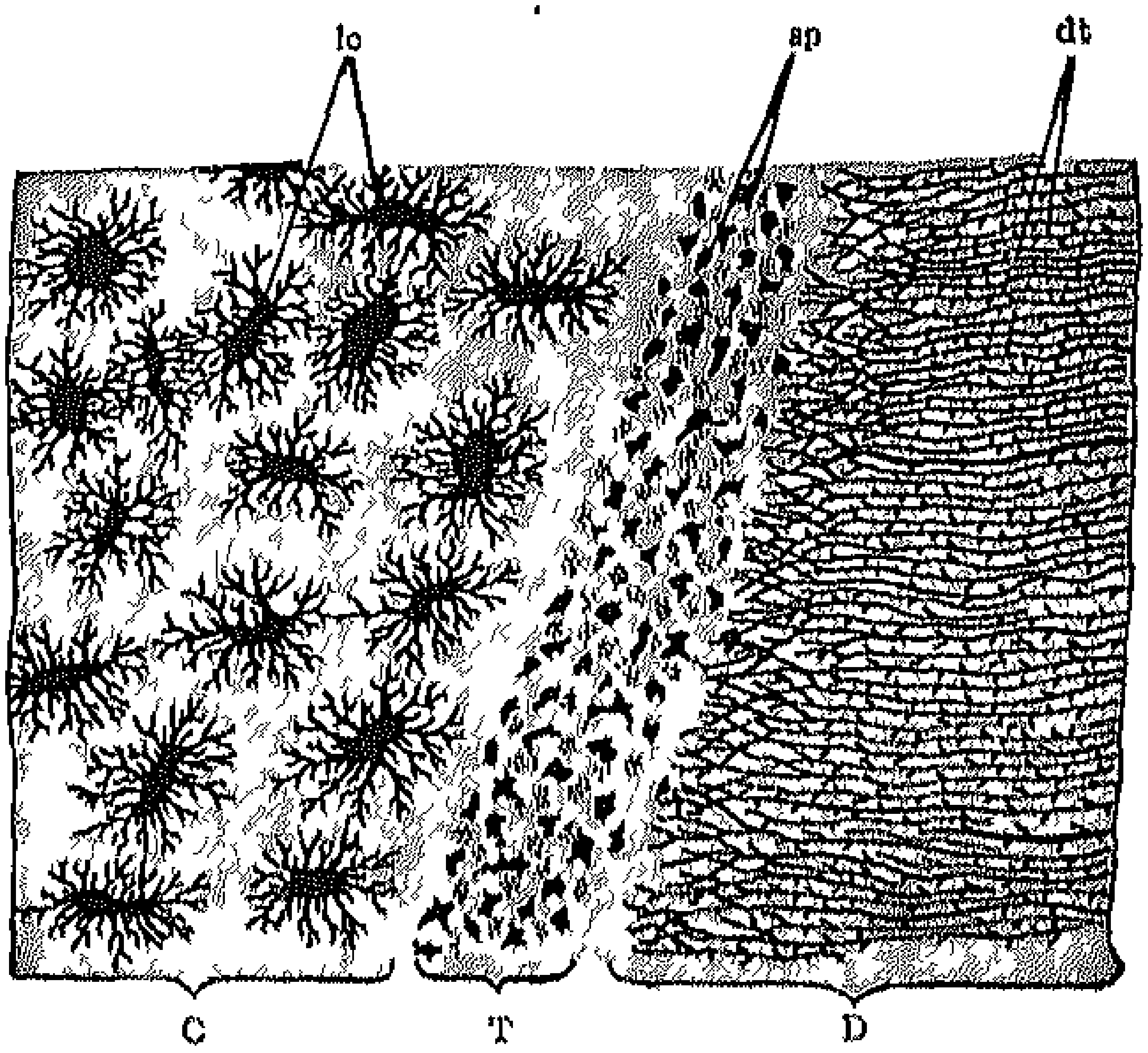


FIG. 116. Section of a tooth at the junction of the dentine and cementum. (D) Dentine. (C) Cementum. (T) Granular area of Tomes. (lc) Lacunae and canaliculi in the cementum. (sp) Spaces in Tomes' area. (dt) Dentinal tubules.

The lacunae are occupied by cement cells (cementocytes) whose protoplasmic processes extend through the canaliculi. The lacunae and canaliculi are similar to those observed in bone, except that they are larger and coarser.

Cementum may be formed at any time during the life of the tooth. It provides an anchorage for the fibers by which the tooth is fixed in the alveolus. Whenever the fibers become loosened so that there is an undue increase in the movement of the tooth, new deposits of cementum are laid down and a firmer fixation of the tooth is established. This type of hyperplasia requires the cementum to have a high vitality and does not occur in periclasia.

DENTAL PULP. The dentine encloses a considerable cavity (*pulp cavity*). This communicates with the exterior by means of a canal extending through the root of the tooth (*root canal*). The canal opens through an aperture known as the *apical foramen*. The pulp cavity contains mesenchymal connective tissue, the *dental pulp*, which consists of stellate or fusiform cells with numerous branched processes. The intercellular spaces are occupied by a fluid matrix in which a number of delicate collagenous fibers are present. The dental pulp also contains many nerves and blood vessels. The wall of the pulp cavity is lined by columnar cells, the *odontoblasts*, that are arranged perpendicular to the wall. Protoplasmic processes from these cells extend into the dentinal tubules as the dentinal fibers of Tomes.

The dental pulp apparently exists for the upkeep of the dentine. Some evidence has been provided to show that fluids from the pulp

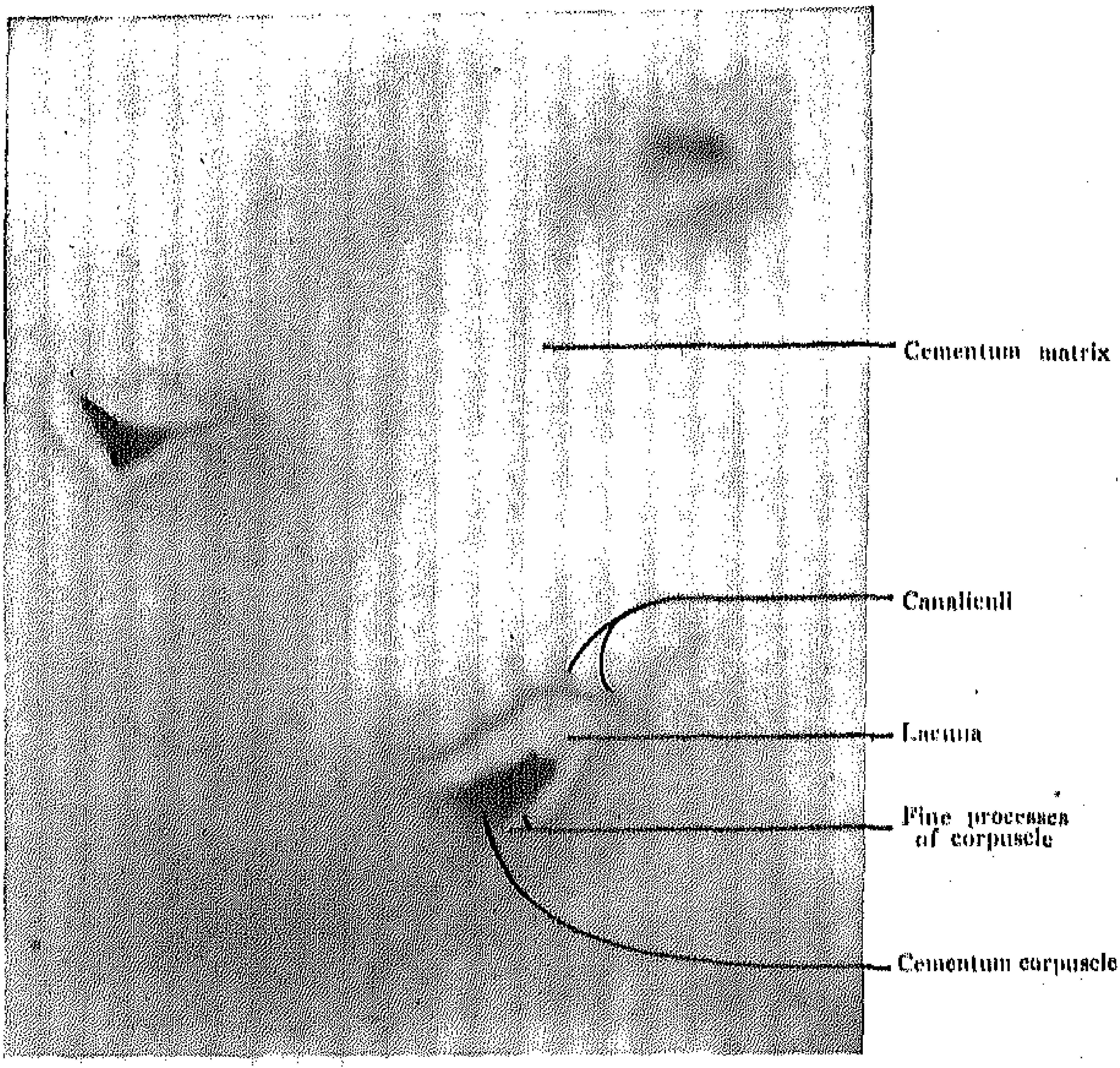


FIG. 117. Oil immersion photomicrograph of three cementum corpuscles, each in its lacuna. Note the tiny radiating lacunar canals (canaliculi), which contain fine processes from the corpuscles. The matrix is made up of fine connective tissue fibrils, into which inorganic salts are precipitated during the calcification processes. Cementum corpuscle processes are directed toward the periodontal membrane. From a ground section of a human molar. Photographed at 2000 ×. (Courtesy, Dr. B. O. A. Thomas, University of Washington Dental School.)

cavity may pass through the dentine and may even be diffused through the enamel. Whenever the dental pulp has been destroyed, the dentine undergoes degenerative changes and the character of the enamel may be profoundly altered.

THE PERIDENTAL MEMBRANE. The space between the cementum and the bone of the alveolar wall is filled with connective tissue. This constitutes the *peridental membrane*, which is continuous

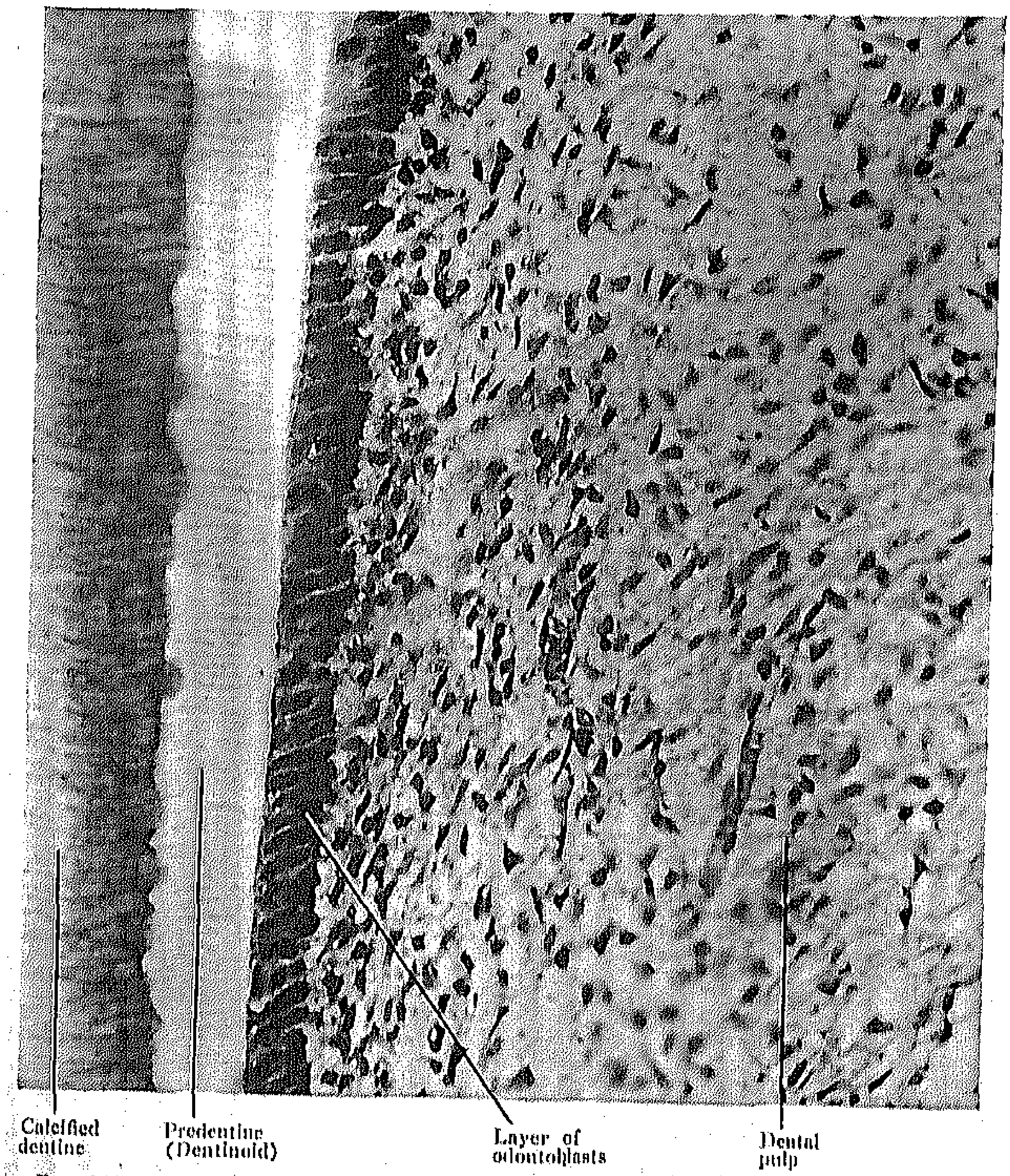


FIG. 118. Human premolar tooth. This demonstrates the formation of dentine. The tall columnar odontoblast cells are well shown, as is the layer of uncalcified dentine matrix (predentine), and the calcified dentine. An area of the young pulp tissue is also clearly demonstrated. Photographed at 440 X. (Courtesy, Dr. B. O. A. Thomas, University of Washington Dental School.)

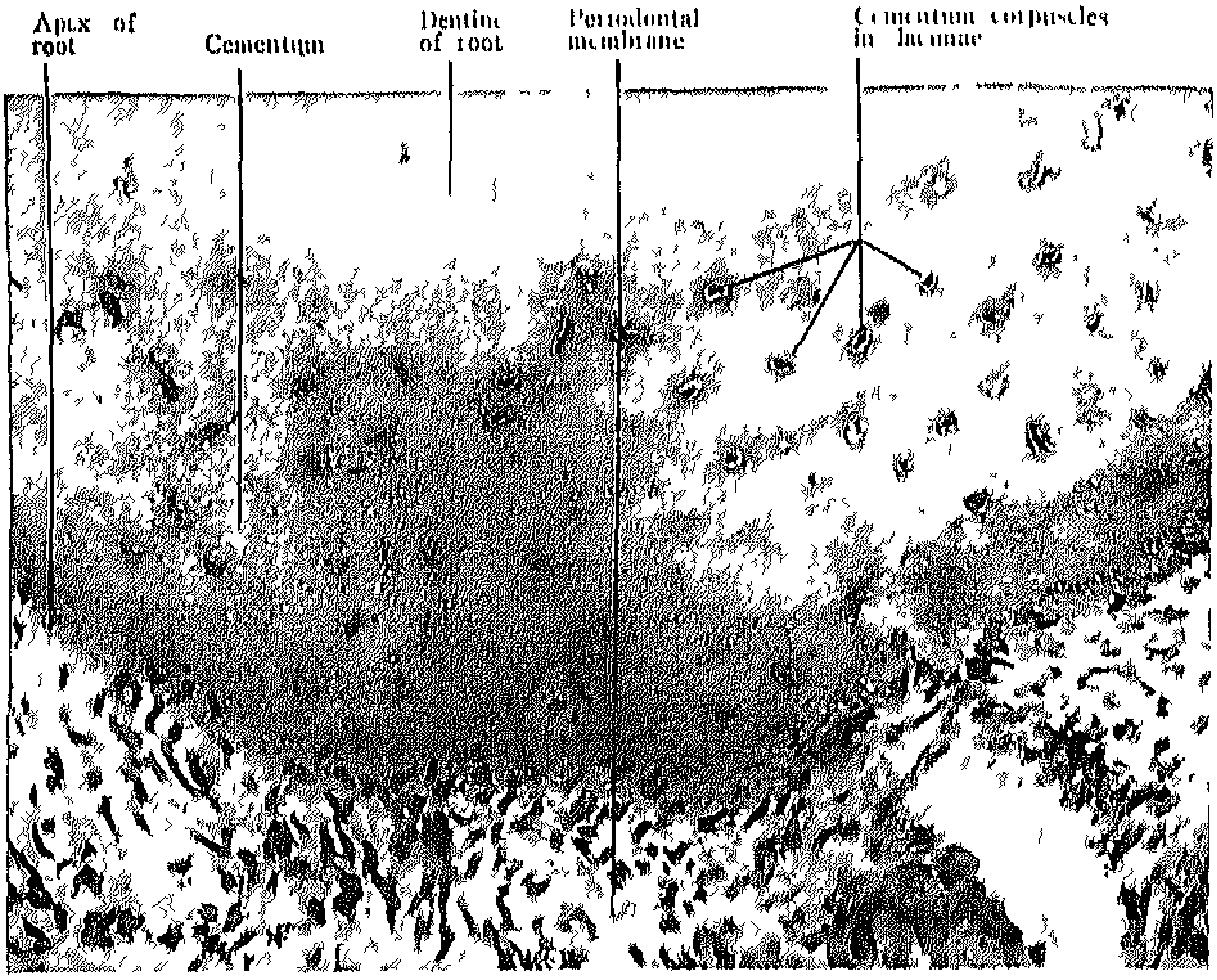


FIG. 119. This photomicrograph includes the tip (apex) of the root of a fully formed tooth, and a portion of the periodontal membrane (fibrous connective tissue) which serves to attach the cementum to the alveolar bone. Several cementum corpuscles, in their lacunae, are well shown. (See higher magnification of cementum corpuscles also.) Cross section showing the three layers of the periodontal membrane seen in the growing tooth germ of humans. Photographed at 400 ×. (Courtesy, Dr. B. O. A. Thomas, University of Washington Dental School)

with the connective tissue of the gum (gingiva) at the alveolar crest. Its fibers intermingle with those of the periosteum of the bone and also with the pericementum. Between these layers the tissue is more or less loosely arranged to provide for the passage of blood vessels and lymphatics. Some of the fibers are in the form of bundles which extend from the bone of the alveolar wall to the cementum about the root of the tooth and the ends of the fibers are embedded in both. These bundles of fibers are known as the dental ligaments. The dental ligaments are so directed that they enable the tooth to resist pressure and also to fix it more firmly in the alveolus.

Blood vessels to the tooth enter the root canal through the apical foramen and extend into the pulp cavity, where they break up into numerous anastomosing branches. These vessels have exceedingly thin walls and may become greatly distended by increased pressure of the blood. When these distended vessels press upon the delicate nerve fibers which lie between them, severe pain results.

The alveolus is supplied with blood vessels which enter it by passing over the alveolar crest, or through channels in the bone. It also receives branches from the vessels which enter the tooth through the apical foramen. These branches unite to form a network, thus assuring the peridental membrane a rich supply of blood.

From three to six nerve filaments enter the tooth, following the course of the blood vessels through the root canal. In the pulp cavity the fibers break up into numerous delicate fibrils which end in relation to the odontoblasts. So far as is known there are no nerve fibers in the dentinal tubules; the failure to demonstrate their presence, however, may be due to faulty techniques.

THE DEVELOPMENT OF THE TEETH. The first indication of tooth development is evidenced by a thickened epithelial ridge (*dental ridge*) which appears during the sixth week of embryonic development along the future alveolar border of the jaw. By the continued proliferation of the cells of this ridge a shelflike structure is formed *(dental lamina)* which pushes downward into the subepithelial mesodermal tissue. This lamina first appears anteriorly, from which point it grows progressively backward. A series of buds at ten different points, corresponding to the future position of the deciduous teeth, are formed on the border of the dental lamina by the continued growth of the epithelial tissue. These buds expand to form a cap-shaped structure and later appear as a bell-shaped structure. This briefly traces the development of the *enamel organ*. The enamel organ not only gives rise to the tooth enamel but it also determines the shape (number of cusps, etc.) of the crown of the tooth.

As seen in section, an enamel organ consists of a layer of cuboidal cells which form its upper and side walls (*outer enamel cells*). Continuous with the outer enamel cells, but pushed upward so that they lie partly within them, is a row of columnar cells (*inner enamel cells*). At first the cells enclosed by the outer and inner enamel cells are similar to those which form the superficial cells of the dental ridge, of which they are the counterpart. As the development of the enamel organ progresses, these cells are pushed apart by an accumulation of fluid and assume a stellate shape, their protoplasm being extended in the form of a number of branched processes. This tissue is known as the *stellate reticulum* and its appearance is not unlike that of the primitive mesenchyme. The cells of the stellate reticulum, together with the fluid which fills the intercellular spaces, constitute the *enamel pulp*. The mesodermal cells are aggregated to form a moundlike structure, the *dental papillae,* which lies immediately beneath the enamel organ and which pushes the inner enamel cells upward so that they come to lie within the outer enamel cells.

With the continued development of the enamel organ, the outer

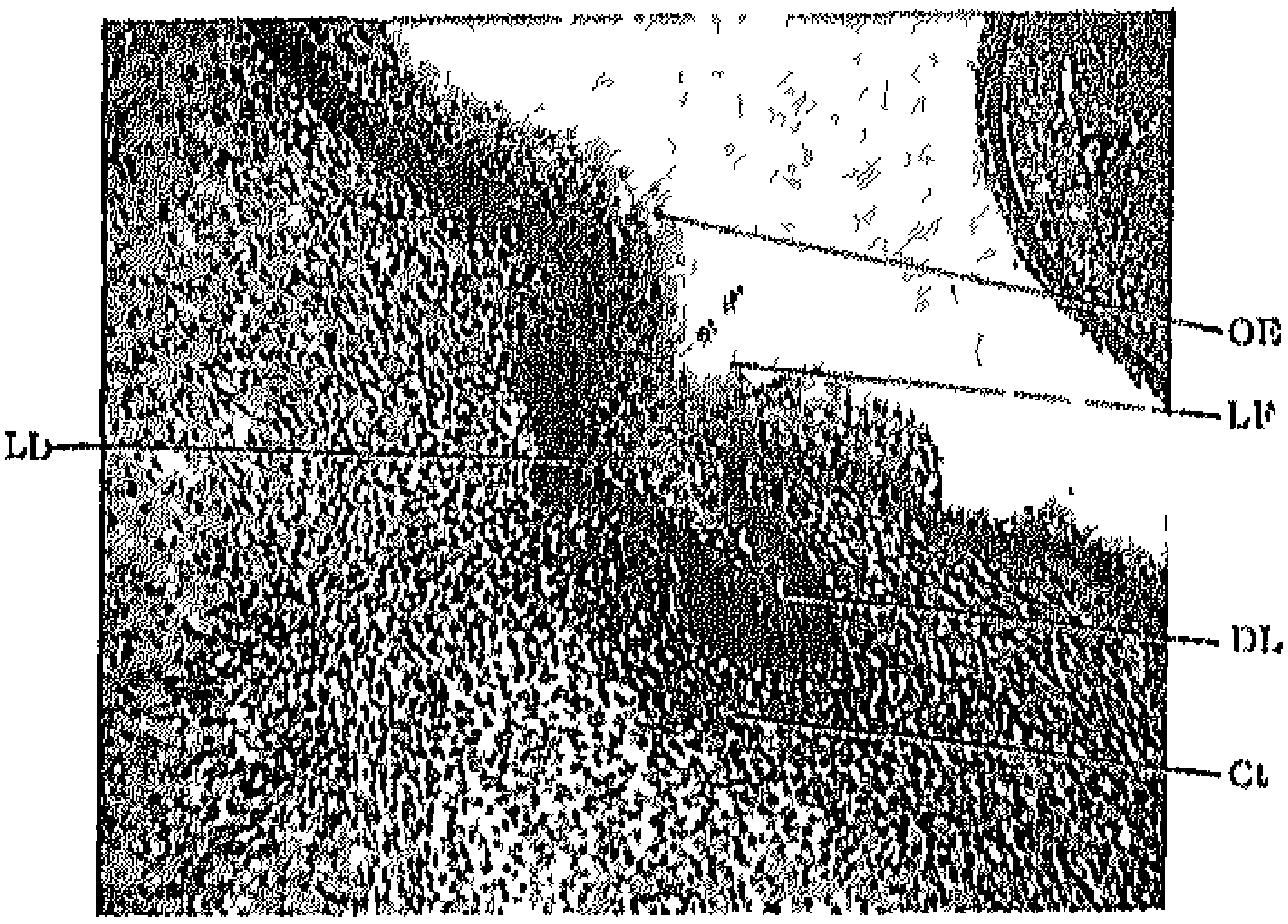


FIG. 120. Splitting of the dental ledge. (DL) Dental lamina, expanding at its lower edge to form the enamel organ. (LF) Labio-dental furrow. (LL) Labial lamina. (OE) Oral epithelium. (Ct) Condensation of the mesoderm about the forming enamel organ—the first indication of the dental papilla. (T) The tongue. Photomicrograph.

enamel cells become thin and flattened. The inner enamel cells assume a tall, columnar form to become the ameloblasts by which the substance of the enamel is deposited. Between the stellate reticulum and the inner enamel cells, several layers of flattened squamous cells appear. This layer of cells is called the *stratum intermedium* and is esssential for the formation of the enamel. It is not present in the root region. Mesodermal cells from the dental papilla extend around the enamel organ and form the *dental capsule*. Immediately adjacent to the ameloblasts, the cells of the papilla become elongated, cylindrical odontoblasts which are active in the formation of the dentine. A narrow space between the ameloblasts and odontoblasts is filled with a light homogeneous substance to which has been applied the term, *membrana performata*. However, this is not a distinct membrane, but the first layer of *predentine*, or the organic base which becomes the dentine proper by the addition of successive layers and by calcification. During the entire period in which dentine is being formed, a similar layer is to be observed between the odontoblasts and the calcified dentine. It is necessary that dentine is first formed before enamel can be laid down.

The enamel first appears as a densely calcified tissue on the external surface of the dentine with the tall, columnar, ameloblasts resting on its outer surface. During the growth of the tooth, the dentine extends little below the enamel over the sides of the dental papilla. A layer f enamel matrix lies between the calcified portion of the enamel and e ameloblasts. As the newer layers of pre-enamel are deposited, the lder layers become true enamel by the deposit of calcium salts. Delicate, protoplasmic processes, the *enamel processes of Tomes*, extend from the ameloblasts into the substance of the pre-enamel. It is believed that in some way, these processes influence its calcification.

By the time the formation of the enamel and dentine has progressed to the cementoenamel junction, the enamel pulp has become so greatly reduced that the inner and outer enamel cells below the cemento-enamel lie close together and are fused to form the cervical loop. This cervical loop continues to grow downward over the sides of the dental papilla in the future root region. Thus a two-layered epithelial structure is formed between the dental papilla and the connective tissue of the dental capsule *(sheath of Hertwig)*. This structure provides a form within which the root of the tooth is developed. The mesodermal tissue of the dental papilla is gradually transformed into the embryonal connective tissue of the dental pulp.

The enamel is laid down as bundles of rodlike, prismatic structures; each enamel cell being engaged in depositing the substance of the rod which is formed immediately beneath it. The rods begin at the dento-enamel junction and as the growth of the enamel continues, the surface area of the crown increases rapidly. Groups of parallel rods are cemented together into bundles, but the bundles themselves do not always lie parallel, instead they cross one another at different angles.

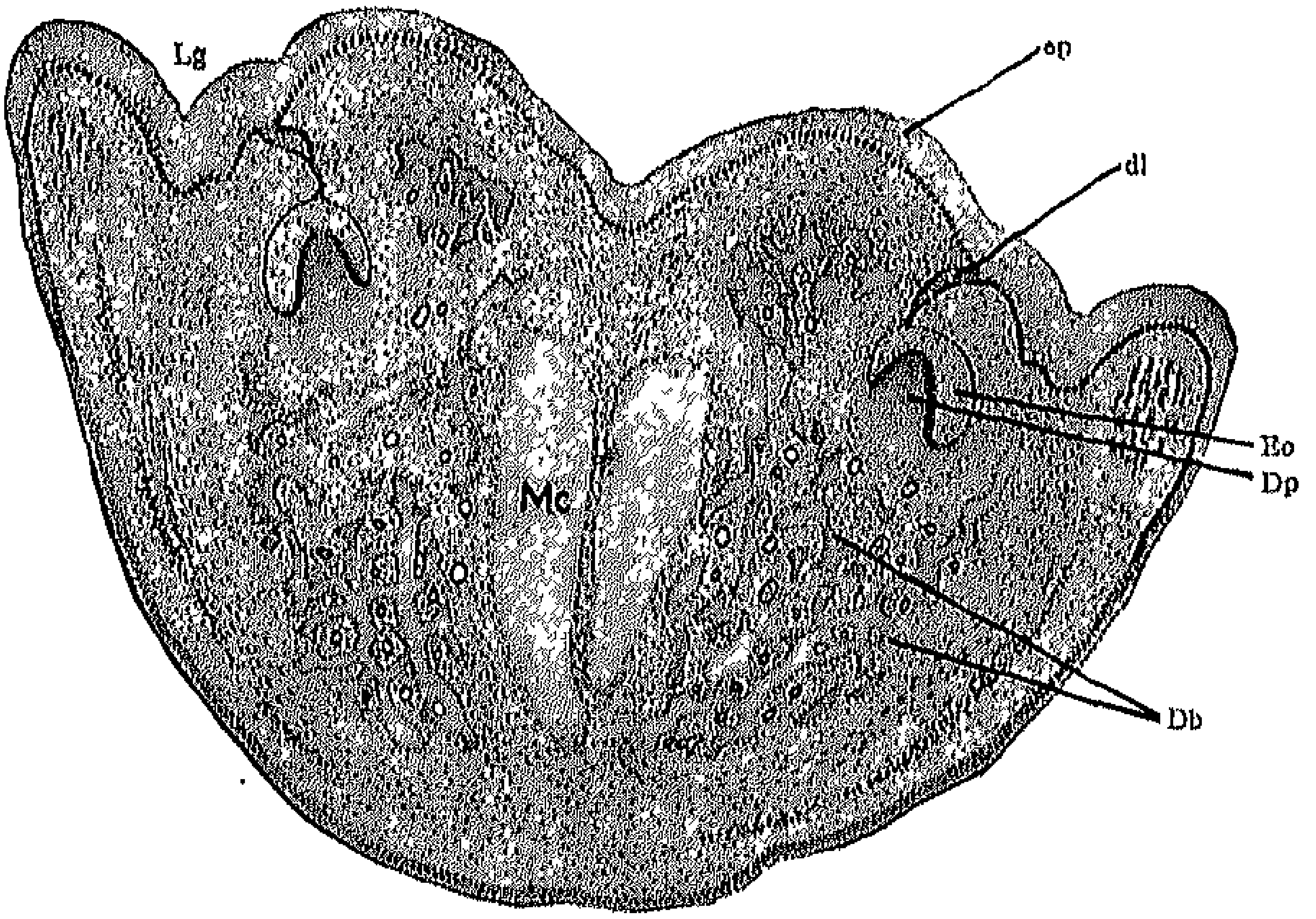


Fig. 121. Section through the mandible of an early pig embryo just posterior to the symphysis of the jaw. (Mc) Meckel's cartilage. (Eo) Enamel organ. (Dp) Dental papilla. (Db) Plates of developing bone forming the mandible. (dl) Dental lamina. (Lg) Labial groove. (ep) Epithelium of the buccal cavity.

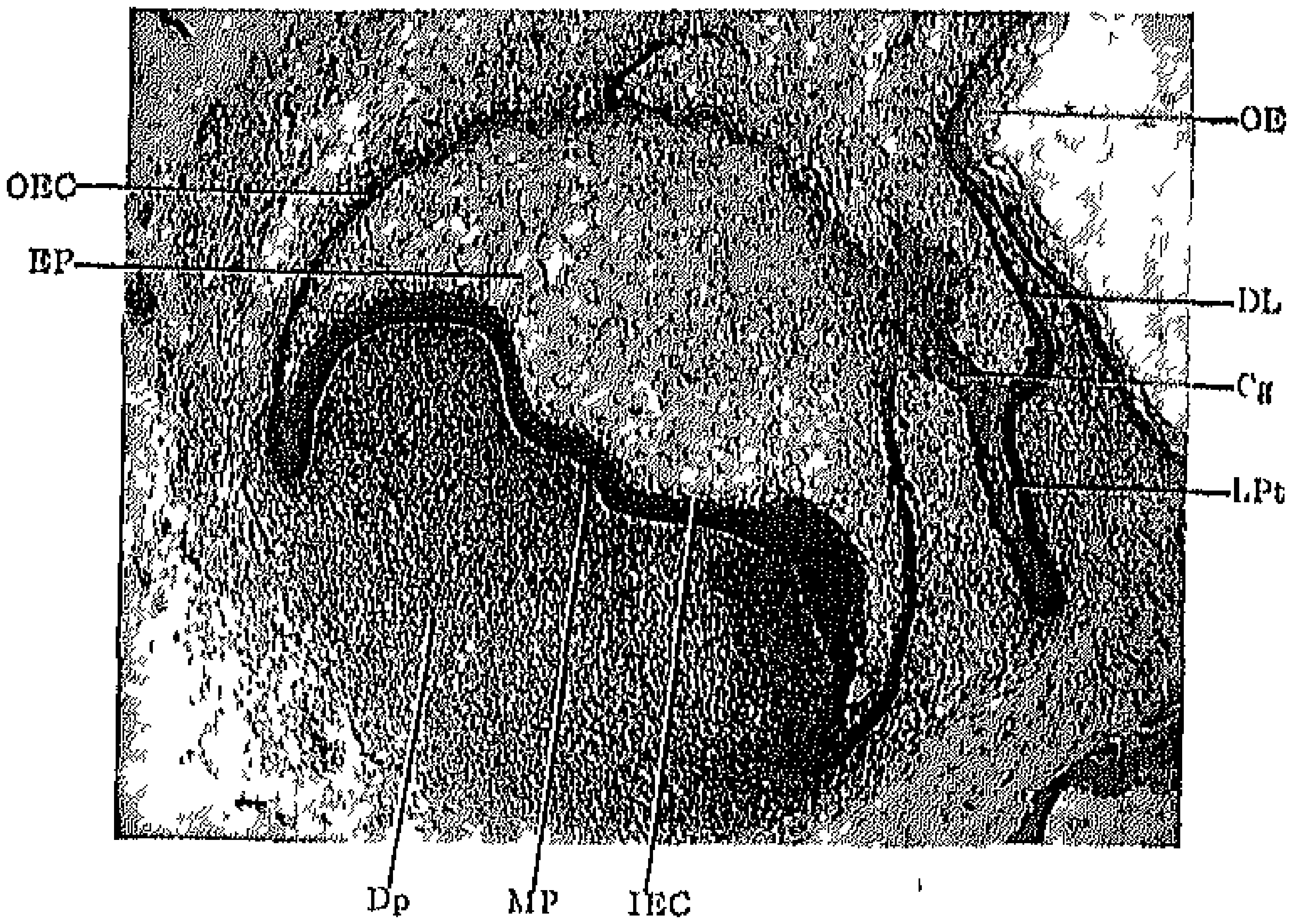
This irregular arrangement occurs in the region of the crown. In the area of the cusps where the enamel is thickest, this arrangement is even more irregular and the bundles of rods twist about one another forming what is known as *gnarled enamel*. Toward the neck, where the enamel is considerably thinner, the rods are parallel to one another from the junction to the surface. Such areas are known as *straight enamel*.

The enamel rods are held together by a substance which is considerably softer than the enamel itself and which is called the *enamel cement*. When viewed microscopically, the rods are seen to be crossed by transverse markings which are due to the deposit of the substance of the enamel in successive layers.

Shortly after the tooth germ (enamel organ and dental papilla) is fully developed, a second lamina is formed by epithelial cells which grow out in the lingual direction from the lamina of the deciduous teeth. This is the lamina of the permanent teeth. Buds which are formed on the border of this lamina develop into enamel organs, the process following the same course as in the development of the deciduous teeth.

The capsule of the tooth is connected with the surface of the gum *(gingival surface)* by a cord of dense fibrous tissue. This cord acts as a guide for the tooth when it erupts. A similar connection exists between the capsule of the permanent tooth and that of the deciduous tooth. The bony structure of the jaw develops about the germs of both the permanent and deciduous teeth but does not penetrate these fibrous cords. Thus, while a narrow open space remains between the tooth and the surface of the gum indicating the path for eruption, nevertheless, erosion of some of the intervening bone occurs as a result of pressure caused by the growing tooth. As the deciduous tooth rises above the gum, the germ of the permanent tooth comes to lie more nearly beneath it.

The cementum does not appear until after the crown has emerged through the surface of the gum and a considerable development of the dentine of the root has been accomplished. The connective tissue of the dental capsule lies between the bony wall of the alveolus and Hertwig's sheath, within which the root of the tooth is formed. The sheath is a two-layered structure consisting of an extension, by growth, of the inner and outer enamel cells. The inner enamel cells of the sheath lose their power to form enamel. The odontoblasts adjacent to this layer, however, continue to deposit the dentine which lays the foundation of the root. The sheath of Hertwig breaks up into fragments, most of which are resorbed although some of the epithelial cells of the sheath may remain in the peridental membrane and form epithelial islands known as "epithelial rests."



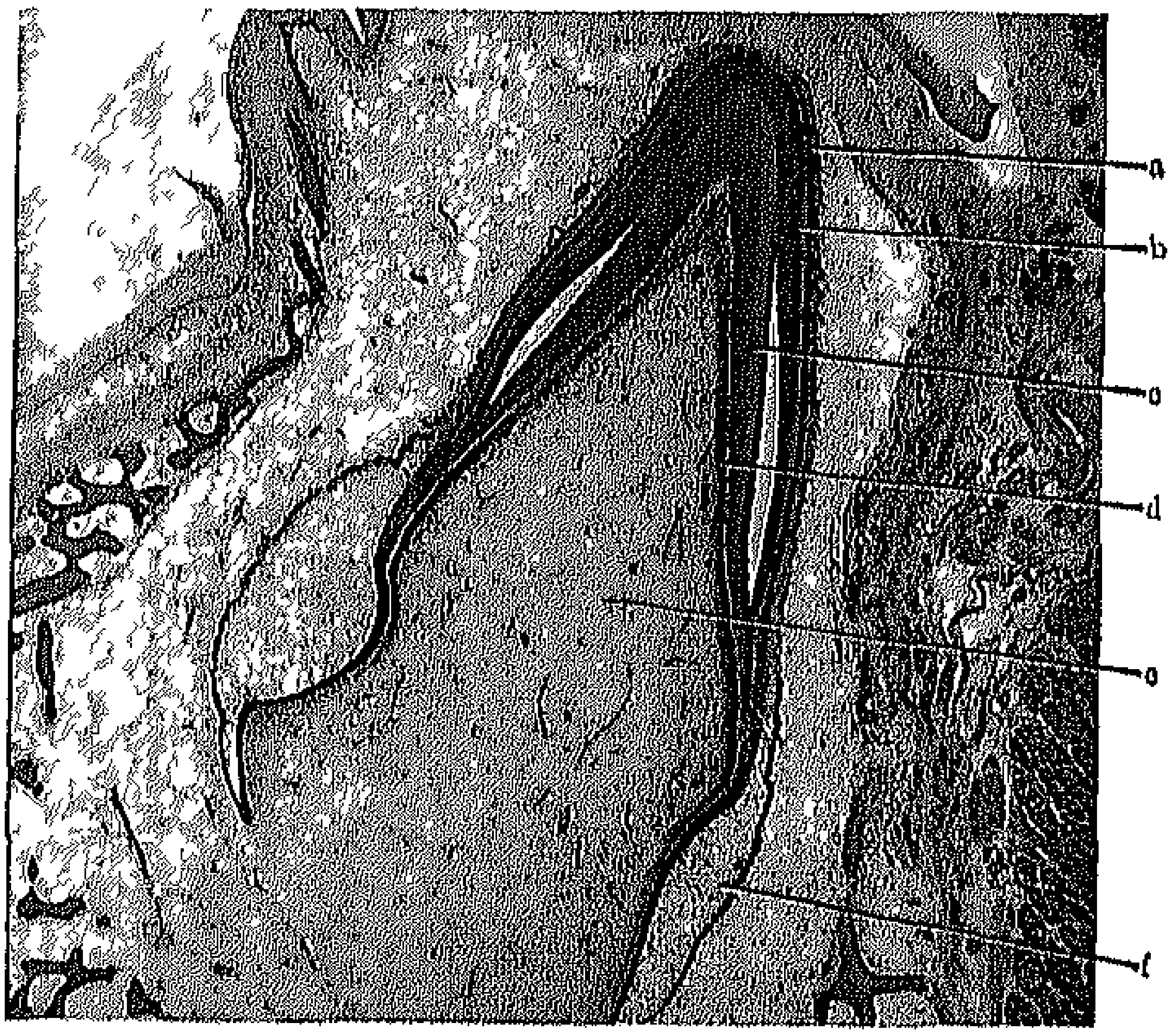


Fig. 122. *(Top)* Tooth germ showing the enamel organ and the lamina of the permanent tooth. (Cg) Cingulum. (DL) Dental lamina. (Dp) Dental pulp. (EP) Enamel pulp. (IEC) Inner enamel cells. (LPt) Lamina of permanent tooth. (MP) Membrana preformative. (OE) Oral epithelium. (OEC) Outer enamel cells. Photomicrograph.

Fig. 123. *(Bottom)* Developing enamel and dentine. (a) Ameloblasts. (b) Enamel. (c) Dentine. (d) Odontoblasts. (e) Dental pulp. (f) Hertwig's sheath. Photomicrograph.

With the fragmentation of Hertwig's sheath, the connective tissue of the capsule *(peridental membrane)* is brought into contact with the dentine of the root upon which its fibers form a compact layer, the *pericementum*. An organic cementing substance is deposited around these fibers by transformed fibroblasts, the *cementoblasts*. The latter probably also are important in the calcification of the "cementoid" substance. As the cementum develops, some of the cementoblasts become incorporated in its substance where they remain as the *cementocytes*. As indicated above, the portion of the dental capsule which remains between the root of the tooth and the wall of the alveolus, becomes the peridental membrane.

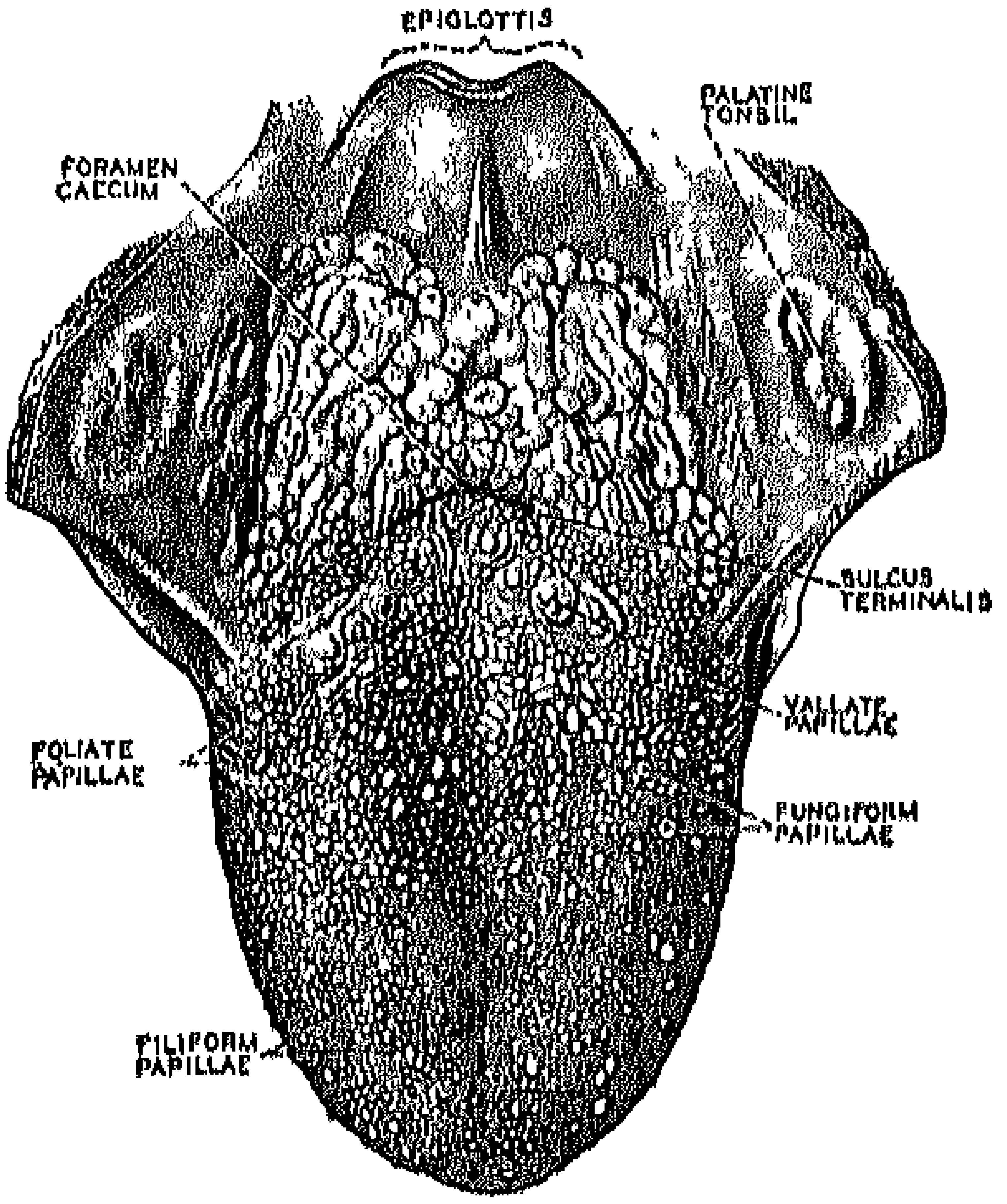


Fig. 124. The dorsum of the tongue. (Courtesy, Neal and Rand: "Comparative Anatomy," Philadelphia, The Blakiston Company.)

THE TONGUE

The tongue is a large, muscular organ which almost completely fills the oral cavity. Its attachments are to the symphysis of the mandible, the floor of the oral cavity, and to the hyoid bone. It presents two main divisions, a *body* and a *base* or root. The body lies in the oral cavity and anteriorly it ends in a more or less free portion, the *tip*.

The tip is bound to the floor of the oral cavity by a thin band of connective tissue, the *frenulum*. The upper surface or *dorsum* is roughened by the presence of numerous elevations of its epithelium, the *lingual papillae*. The base is more or less vertical in position and forms the anterior wall of the oropharynx. The division between the dorsum and the base is indicated by a faintly marked V-shaped furrow, the *sulcus terminalis*. The dorsum is divided into lateral halves by a longitudinal furrow, the *lingual sulcus*, which extends from the tip to the base.

When viewed in section, the body of the tongue is seen to consist principally of bundles of striated muscle fibers which are disposed in three planes: vertical, horizontal and longitudinal. These fibers represent two distinct groups of muscles: those which have their origins external to, and their insertions within, the body of the tongue *(extrinsic muscles)*; and those which have both their origins and insertions within the tongue *(intrinsic muscles)*.

The extrinsic muscles are as follows: the *genioglossus*, which arises from the genial tubercles on the posterior surface of the mandible, its fibers spreading out fanwise to end in the connective tissue of the dorsum; the *hyoglossus*, which arises from the hyoid bone and enters the body of the tongue lateral to the genioglossus; the *styloglossus*, which takes its origin from the tip of the styloid process and enters the body of the tongue in two bundles, one above the other, on its lateral aspect; the *palatoglossus*, which originates in the anterior portion of the soft palate and enters the tongue between the upper and lower bundles of the styloglossus.

The intrinsic muscles are: the *transversus*, the fibers of which extend from the lingual septum to the sides of the tongue; the *longitudinalis*, its fibers extending in a superior and an inferior bundle from the tip to the base of the tongue; and a *verticalis*, the fibers of which pass upward, crossing those of the transverse muscle at right angles.

The surface of the tongue is covered by a *mucous membrane* which consists of an epithelial layer and a tunica propria. The epithelium is a thick layer of stratified squamous epithelium which is continuous with the epithelial lining of the mouth. It rests on a narrow tunica propria in which may be seen small aggregations of lymphocytes. The connective tissue fascia which surrounds the muscles and gives support to the organ is continuous with the deep layer of the submucosa where it is present. The *submucosa* contains a variable amount of fat and supports glands. It consists of closely interwoven connective tissue bundles which form a dense investment of the muscular portion of the tongue, the *lingual fascia*, to which the muscle fibers are attached. The *lingual septum* is an extension of the lingual fascia and extends from the tip of the tongue to the hyoid bone. This septum divides the tongue into identical lateral halves.

The submucosa appears on the lateral sides and the under surface of the tongue (on its upper surface the mucosa is in direct relation to the connective tissue fascia) where it lies immediately beneath the mucosa. It consists of a relatively thick layer of loosely arranged collagenous and elastic fibers.

The mucosal surface on the dorsum and upper part of the lateral surfaces of the tongue are raised into a number of moundlike elevations known as *lingual papillae*. These papillae are formed by projections of the subepithelial connective tissue which carry with it the mucosal layer. These papillae, consisting of a connective tissue core and a mucosal covering, extend above the general level of the lingual surface. The connective tissue which forms the core of the elevation is known as the *primary papilla*. Smaller elevations, arising from the surface of the primary papilla and penetrating the deep surface of the epithelium, are known as *secondary papillae*.

These large "taste" papillae, which are elevations of both the tunica propria and the epithelium, should not be confused with the papillations found in relation to stratified squamous epithelium which are connective tissue papillations which project into the deep surface of the epithelial layer.

There are three types of lingual papillae: the *filiform*, the *fungiform*, and the *circumvallate*. A fourth type consisting of a series of leaflike folds, occurs on the sides of the tongue in infants *(foliate papillae)*, but are indicated only by faint lines in the adult.

FILIFORM PAPILLAE. These are the most numerous of the lingual papillae and are arranged in parallel rows, extending from the lingual sulcus to the sides of the dorsum of the tongue. They consist of an epithelium which rests on an elevation of the subepithelial tissue. Two or three secondary papillae arise from the surface of the primary papilla. The cells of the epithelium above the secondary papillae become elongated and cornified, forming slender threadlike processes.

FUNGIFORM PAPILLAE. Fungiform papillae appear singly or in groups of two or three between the rows of filiform papillae, and are especially abundant on the tip and over the sides of the dorsum of the tongue. They are broad and rounded at the top and constricted at the base, which gives them the mushroomlike appearance from which their name is derived. They are richly supplied with blood vessels and not so completely keratinized, which causes them to appear as bright red dots scattered over the surface of the tongue. Taste buds are frequently present on the sides of the fungiform papillae.

CIRCUMVALLATE PAPILLAE. Circumvallate papillae resemble the fungiform papillae in form, but are considerably larger and are set in deep depressions, or pits, in the epithelium. When viewed from the surface, this gives them the appearance of being surrounded by a furrow or *vallum*. The stratified epithelium is quite thick over the surface of the papilla, but becomes much thinner on its sides. The circumvallate papillae vary in number from 8 to 12, and are arranged in a single, V-shaped row in front of the sulcus terminalis. A number of secondary papillae arise from the primary papilla and penetrate the deep surface of the epithelium without, however, producing any corresponding elevations of its surface.

Taste buds are present in the epithelium on the sides of the circumvallate papillae and also in the epithelium on the adjacent wall of the furrow. They are *neuroepithelial* structures consisting of epithelial cells which have been modified for the reception of gustatory sensation. The buds consist of two kinds of cells, the outer or *sustentacular cells*, which enclose and support the inner or *gustatory* cells. The gustatory cells are rodlike structures, their protoplasm forming a bulge in the middle of the cell for the accommodation of the nucleus. A slender, hairlike process extends from the summit of each rod through a small opening in the epithelium above the bud, the *gustatory pore*. The taste buds are considerably lighter in color than the surrounding epithelium and in appearance have been likened to a Chinese lantern. They are found not only in the tongue, but also in the epithelium covering the soft palate and on the surface of the epiglottis.

Papillae are not present on the epithelium over the base of the tongue, which is smooth and glistening. Its surface is raised into a number of rounded elevations by masses of lymphoid tissue which are present in the subepithelial tissue and form the lingual tonsil. A number of small, pitlike openings may be seen on the surface of the epithelium which lead into the tonsillar crypts. A large pitlike opening, the *foramen caecum*, is located directly behind the apex of the row

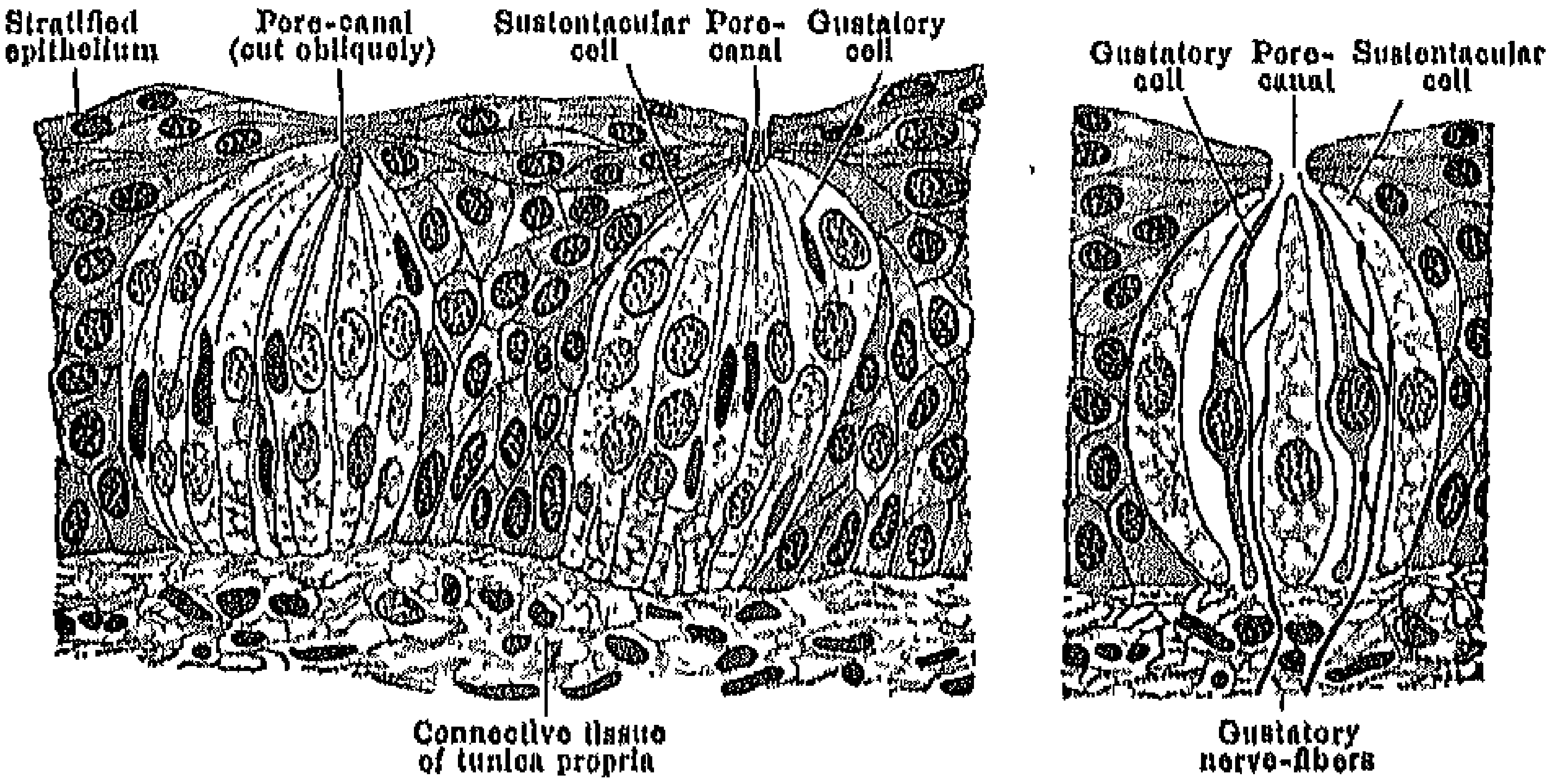


FIG. 125. Taste buds in vertical section. *(Left)* From a vallate papilla. 475 ×. *(Right)* Diagram of the structure of a taste bud. 475 ×. (Courtesy, J. Parsons Schaeffer, Ed.' "Morris' Human Anatomy," Philadelphia, The Blakiston Company.)

of circumvallate papillae. This represents the pharyngeal opening of the obliterated thyroglossal duct.

Both mucous and serous glands are present in the connective tissue investment of the tongue and may be present in the septa between the muscle bundles. The glands are of the tubuloacinar type and are arranged in groups. One group of mucus-secreting glands is located beneath the tip of the tongue (often referred to as the *glands of Blandin*). Groups of serous glands occur in the region of the circumvallate papillae (*glands of von Ebner*). The ducts of these glands open into the floor of the furrow about each papilla. Other glands, located in the body of the tongue, are connected by their ducts with the tonsillar crypts.

The blood supply of the tongue is through the lingual artery, whose branches pass in the connective tissue septa, to be distributed to the muscles and glands. The branches which are located in the submucosa form a plexus of small vessels from which capillary loops xtend into the primary and secondary papillae. The veins by which e blood is returned from the tongue follow, in general, the course the arteries.

The tongue has a rich supply of lymphatics, which originate in the ssue spaces of the submucosa and about the muscle fibers and glands. fine network of lymph capillaries also surrounds the nodules in the ingual tonsil. The structure of the lingual tonsil has been discussed n p. 205.

The tongue is supplied by both sensory and motor nerve fibers. The sensory nerves are those which convey impulses of common sensation such as touch and temperature, and those which convey the special sensation of taste. The fibers of common sensation to the anterior two-thirds of the tongue are from the *trigeminal nerve;* those to the posterior third are from the *glossopharyngeal nerve.* Fibers from the *chorda tympani* supply the taste buds on the anterior portion of the tongue, while those in the circumvallate papillae are supplied by branches from the *glossopharyngeal nerve.* The motor supply of the muscles is through branches from the *hypoglossal nerve.* The walls of the blood vessels and glands are supplied by unmyelinated fibers from the autonomic system.

THE PHARYNX

The pharynx is a membranous tubelike structure which lies behind and below the nasal and oral cavities. Its upper part is membranous and is closely applied to the base of the skull, while its lower part is more or less tubular, with a greatly thickened wall in which the striated fibers of the *pharyngeal constrictor muscles* are present.

It consists of three successive segments: the *nasopharynx,* the *oro-*

pharynx, and the *laryngopharynx*. The nasopharynx lies behind the nasal cavities and above the soft palate. The segment between the soft palate and the hyoid bone is the oropharynx. It communicates anteriorly with the oral cavity. The laryngopharynx extends from the hyoid bone to the lower border of the cricoid cartilage where it continues as the esophagus.

The epithelium which lines the nasopharynx is predominately pseudostratified columnar but contains some areas of stratified squamous. It is a continuation of the respiratory epithelium of the nasal passages. Below the level of the posterior border of the hard palate it merges with the stratified squamous epithelium with which the remainder of the pharynx is lined. As age advances, the pseudostratified columnar epithelium of the nasopharynx may be replaced by the stratified squamous type.

The epithelium rests on a comparatively thick layer of delicate connective tissue fibers in which numerous lymphocytes are present. Here and there the lymphocytes form diffuse aggregations and occasionally appear as small nodules. In the region between the posterior nares and the openings of the Eustachian tubes, the nodules are aggregated to form the *pharyngeal tonsils*. Because of the delicate character of its fibers and the presence of lymphocytes, the subepithelial tissue is regarded as a *tunica propria*.

A well-developed layer of elastic fibers, mostly longitudinal in direction, is interposed between the tunica propria and the adjacent tissue. The elastic fibers extend downward in the pharynx to its junction with the esophagus where they disappear. Striated fibers of the pharyngeal constrictor muscles are present in the posterior and lateral walls. No definite direction can be ascribed to these fibers as they appear in sections, although the inner layer tends to be longitudinal, while the fibers of the outer layer are obliquely directed. Oblique fibers may be found intermingling with the longitudinal fibers of the inner layer.

There is no well-defined submucous layer between the tunica propria and the muscular layers, which are separated by the layer of elastic fibers. Some of the elastic fibers extend outward between the muscle bundles.

The anterior wall of the pharynx is practically devoid of muscular fibers. A distinct submucosa lies external to the tunica propria, from which it is separated by the elastic layer. Mucus-secreting glands are present in the submucosa.

On the posterior wall, external to the muscular layer, is a layer of loose areolar tissue which serves to attach the pharynx to the adjacent structures. Anteriorly, the submucosa merges with the connective tissue of the wall of the larynx.

Mixed mucous and serous glands are present in the region of the nasopharynx. The glands in the submucosa of the laryngopharynx are of the pure mucus-secreting type.

THE ESOPHAGUS

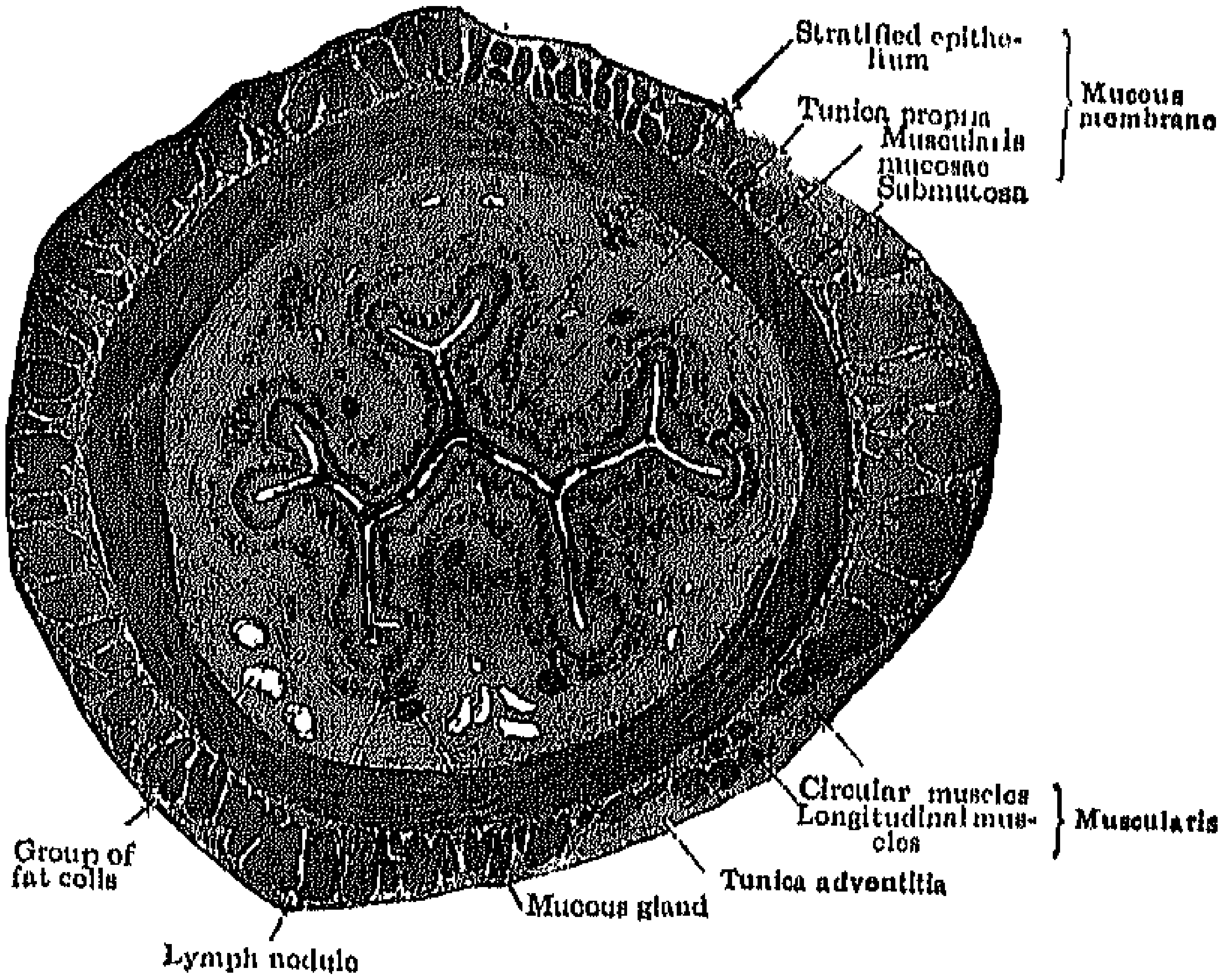
The esophagus extends from the lower end of the pharynx to its junction with the stomach, which takes place a short distance below the diaphragm. It is about ten inches in length. In the upper part of its course it lies behind and a little to the left of the trachea, to which it is bound by connective tissue. For the remainder of its course it lies approximately in the mid-line of the body. The wall of the esophagus consists of five layers: a *mucosa*, *muscularis mucosae*, *submucosa*, *muscularis externa*, and *adventitia* or fibrous layer.

The *mucosa* consists of an epithelium which rests on a tunica propria. The epithelium lining the entire length of the esophagus is a thick layer of stratified squamous epithelium. The superficial cells contain keratin in the form of small granules, but are not cornified like the superficial cells of the epidermis. Its deep surface is penetrated by tall, narrow papillae from the underlying connective tissue. This epithelium rests on a layer of delicate, loosely interwoven fibers of connective tissue, the tunica propria. Lymphocytes are scattered freely throughout the tunica propria and here and there form small, diffuse aggregations which may take the form of nodules.

Separating the tunica propria from the submucosa is a well-defined layer of longitudinally directed smooth muscle bundles, the *muscularis mucosae*. It takes the place of the elastic tissue layer which occurs in the pharynx. In its upper part, where some of the elastic layer extends from the pharynx into the esophagus, the muscularis mucosae consists of small, scattered bundles of smooth muscle. In the middle third of the esophagus these bundles are united to form a thin, but continuous layer. In the lower third this layer increases in thickness and an inner layer of circular fibers may be added.

The *submucosa* lies external to the muscularis mucosae. It consists of coarse collagenous and elastic fibers which give support to blood vessels, lymphatics, and small bundles of nerve fibers. The three layers, the mucosa, muscularis mucosae and submucosa are raised into a series of longitudinal folds when the walls of the esophagus are not distended, which give to the lumen of the tube an irregular outline.

The *muscularis externa*, or muscular coat, lies external to the submucosa. The muscular fibers are arranged in the form of an inner circular layer and an outer longitudinal layer. The fibers of the two layers are gathered into incomplete bundles, between which are thin septa of connective tissue providing a pathway for the passage of blood vessels and nerves. A strongly developed connective tissue septum separates the circular from the longitudinal fibers. In the upper part of



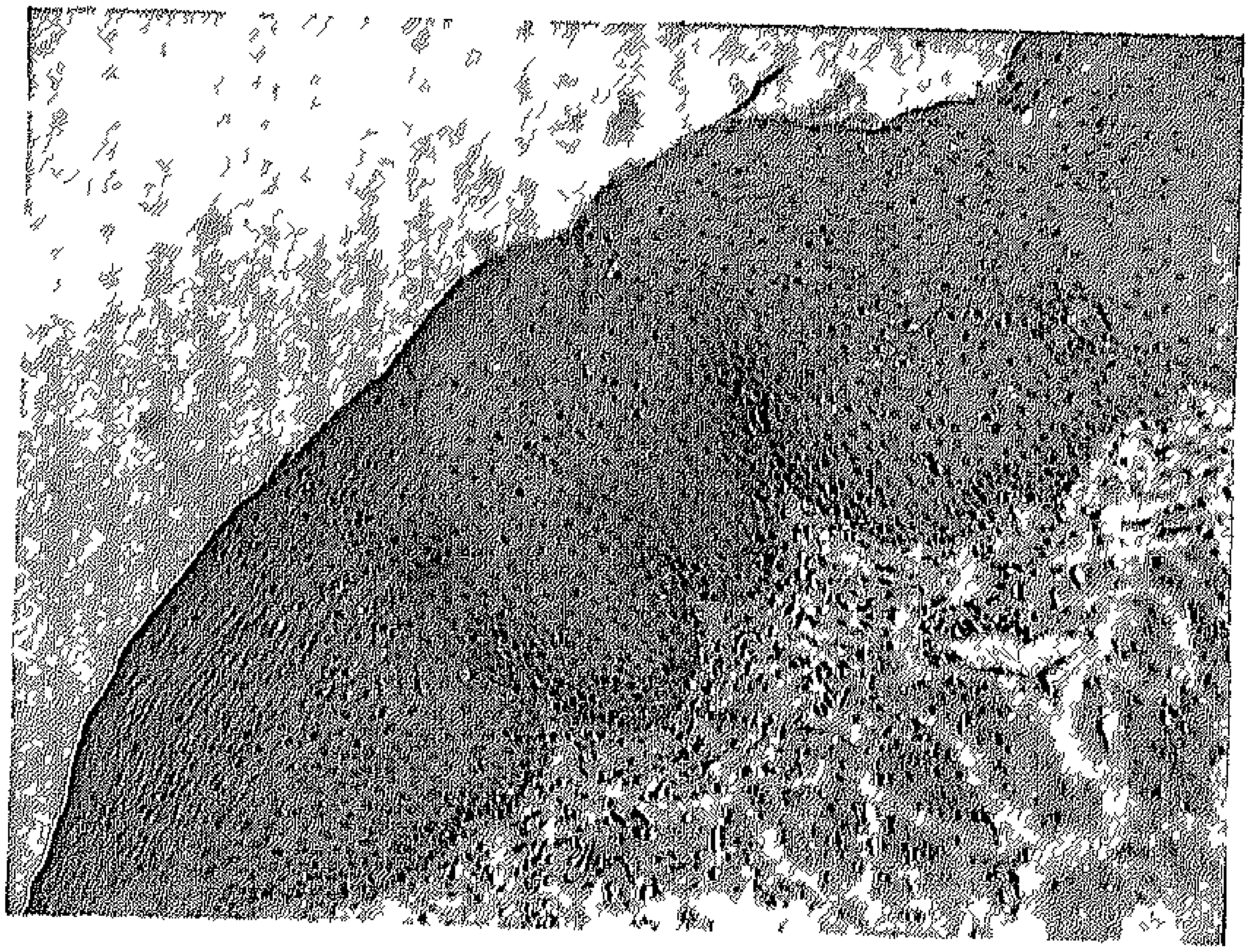


FIG. 126. *(Top)* Transverse section of the upper third of the human esophagus. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

FIG. 127. *(Bottom)* Stratified squamous epithelium from the esophagus (human). Hematoxylin and eosin stain. Photomicrograph.

the esophagus, the muscular coat is composed of striated fibers. Their arrangement as an inner circular and an outer longitudinal layer indicates that they belong to the esophagus and are not a continuation of the pharyngeal muscles. In the middle third of the esophagus, bundles of smooth muscle fibers intermingle with and, to a considerable extent, displace the striated fibers. In the lower third, both the inner and outer layers of the muscular coat consist of smooth muscle fibers. Occasionally, however, a few striated fibers may be present in this region.

The outer coat of the esophagus is an *adventitia*, consisting of loose fibroelastic tissue which contains the blood vessels and nerves passing to the esophageal wall. Small masses of fat cells are frequently present. The adventitia blends with the connective tissue which binds the esophagus to the adjacent structures. Below the diaphragm, the adventitia is replaced by a serous coat which consists of *mesothelium* supported by a substratum of connective tissue.

The glands in the wall of the esophagus are of two kinds: the *deep or true esophageal glands*, and the *superficial or cardiac glands*. The deep glands are mucus-secreting structures located in the submucosa. Their ducts form ampulla-like enlargements below the muscularis mucosae, from which they continue through the tunica propria to open on the surface of the epithelium. They are present throughout the length of the esophagus but are most abundant in its upper and middle thirds. The cardiac glands are so-called because of their similarity to the glands in the cardiac portion of the stomach. They occur in two groups: the upper or superior group is located above the level of the fifth tracheal ring; the lower or inferior group is found just above the junction of the esophagus with the stomach. Because of their

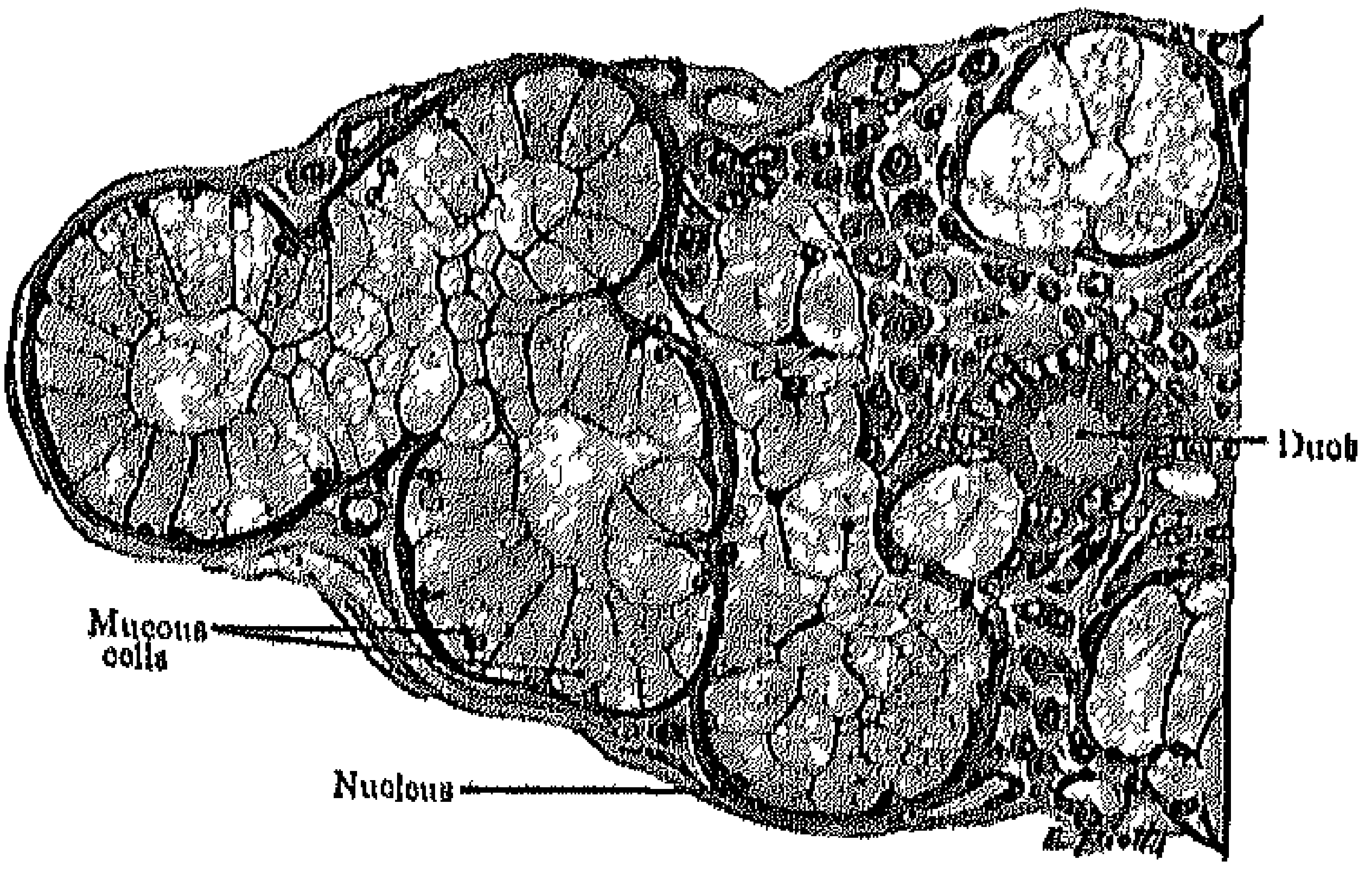


FIG. 128. A section of a deep gland from the esophagus of a nine year old child. Zenker fixation; hematoxylin and eosin. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

location, cardiac glands are not present in every section of the esophagus. The epithelium becomes considerably thinner above these glands and in some cases is said to assume a stratified columnar form. Their ducts divide into several elongated branches, the coiled ends of which lie within, but never pass through, the muscularis mucosae.

Blood is brought to the esophagus by arteries which lie, at first, in the adventitia. The branches of these vessels follow the septa between the muscle bundles, their subdivisions entering the bundles where they break up into capillaries which are distributed among the muscle fibers. Other branches continue into the submucosa where they unite to form a network of larger vessels, from which branches pass through the muscularis mucosae and form a plexus of small vessels whose branches extend into the papillae in the form of capillary loops. The veins arise from the capillaries, the smaller branches uniting to form the larger vessels, which in the main follow the course of the arteries.

Lymphatics occur in the submucosa and in the region of the muscle fibers. The larger lymph vessels, which are formed by the union of the capillaries, join the lymph nodes in the connective tissue about the esophagus.

The striated fibers in the upper part of the esophagus are supplied by myelinated fibers from the vagus nerve. The greater part of the nerve supply, however, is from the autonomic system. The vagal parasympathetic fibers end in relation to groups of ganglion cells located in the septum between the circular and longitudinal layers of the muscular coat, and in the submucosa. Those in the muscular septum belong to the *myenteric (Auerbach's) plexus* from which fibers pass to the muscular layers. Those located in the submucosa belong to the *submucous (Meissner's) plexus* which sends fibers into the muscularis mucosae. Delicate fibers also end between the cells of the epithelium.

THE STOMACH

The stomach is an expanded portion of the alimentary tract and is located between the lower end of the esophagus and the beginning of the small intestine. It lies in the upper part of the abdominal cavity, just below the diaphragm. The shape of the stomach varies considerably, depending on a number of factors, chief among which is the quantity of stomach contents. For a more detailed discussion of the shape, the reader should consult a standard text of anatomy. The stomach is divided into several component parts: (1) The *cardia,* an area about an inch in width, is adjacent to the junction with the esophagus. (2) The *body,* the upper more expanded portion which, in its most cephalad expansion to the left of the cardia, contains the blind saclike expansion called the *fundus.* (3) The *pyloric portion,* the lower region of the stomach which communicates with the small intestine.

The point at which the esophagus enters the stomach shows a marked change in the mucosa both grossly and microscopically. Microscopically it is seen that the stratified squamous epithelium lining the esophagus changes abruptly to the simple columnar epithelium of the stomach. In a fresh specimen this line of transition is readily located by the difference in color between esophageal mucosa which appears whitish, and the mucosal surface of the stomach which is definitely pink due to the thinness of the epithelium and the vascularity of the subepithelial layer. There is little, if any, difference in the deeper layers of the two segments.

The *mucosa* consists of a simple columnar epithelium beneath which is a relatively thick layer of reticular tissue which forms the *tunica propria (lamina propria).* Extending into the upper part of the mucosa are the gastric pits. The pits are wide and shallow in the fundic portion of the stomach, while in the pyloric region they are long and narrow. Opening into the bottom of the gastric pits are the gastric glands which occupy the deeper portion of the mucosa. The reticulum of the tunica propria contains numerous lymphocytes which, here and there, form diffuse aggregations. In the pyloric end of the stomach these aggregations frequently occur in the form of small nodules.

The epithelium of the mucosal surface is made up of a single layer of columnar cells. It extends into the pits and is continuous with the epithelium lining the glands. These columnar cells are tall and the axial portion (toward the lumen) contains mucus. In stained sections it usually shows as a clear, more or less homogeneous area. The cytoplasm of the basal part of the cell is granular and therefore stains more deeply. The appearance of these cells depends to some extent on their secretory activity. The nucleus is round or oval and basally located. There is no definite cuticular border. These cells rest on a distinct basement membrane.

As the cells of the surface epithelium extend into the gastric pits they decrease in height. Many of these cells contain mitotic figures and it has been suggested that new cells are formed in this region which push upward to replace the cells on the surface that are injured or die.

The tunica propria, into which the pits and glands extend, consists of a reticular connective tissue infiltrated with lymphocytes. There is a relatively small amount of tunica propria in the fundic region. Here the glands are simple tubular structures which are arranged so closely that only small amounts of tunica propria extend between them. There is relatively more, however, in the pyloric portion, since in this region the glands are branched and are not so compactly arranged.

The *muscularis mucosae* is interposed betwen the tunica propria and the submucosa. It is usually longitudinally arranged bundles of smooth muscle fibers, but in some instances three poorly defined layers of fibers can be observed: an inner circular, a middle longitudinal, and an outer circular layer.

The *submucosa* consists of loosely interwoven collagenous and elastic fibers in which blood vessels, lymphatics, small bundles of nerve fibers, and Meissner's plexus are present.

The *muscular coat (muscularis externa)* consists of smooth muscle fibers arranged in an inner oblique, a middle circular, and an outer longitudinal layer. The circular layer is the most strongly developed and in the region of the pylorus shows a marked increase in thickness to form the pyloric sphincter. The longitudinal layer is best developed along the lesser curvature and becomes thinner as it spreads out over the expanded wall of the stomach. The longitudinal fibers form a more definite layer in the region of the pylorus. The inner oblique fibers do not form a continuous layer, but appear as scattered bundles, which are best developed in the fundus. The bundles become smaller and less numerous toward the pyloric antrum and finally disappear.

The *serosa* is a continuation of the peritoneal lining of the abdominal cavity. It extends over the gastric wall as a layer of thin mesothelial cells supported by a substratum of connective tissue. It contains the blood vessels, nerves, and lymphatics which supply the wall of the stomach.

Three kinds of glands are included in the gastric mucosa: the *cardiac glands*, the *gastric glands*, and the *pyloric glands*. There are no sharply defined boundaries to the areas which these glands may occupy. Where two such areas meet, the glands intermingle with possible transition forms occurring among them.

CARDIAC GLANDS. The cardiac glands are found in the cardiac portion of the stomach. They are branched tubular glands, which closely resemble the cardiac glands described for the esophagus. They are located in the tunica propria and their tubular branches, secreting portions of the glands, are located just internal to the muscularis mucosae. The epithelium lining the tubules is continuous with the epithelial lining of the stomach. The secreting cells are clear, with basally located nuclei, and produce a modified mucoid material.

GASTRIC GLANDS. The gastric glands are located in the fundus and in the greater part of the body of the stomach. They are simple tubular structures which extend the entire depth of the mucous membrane to the muscularis mucosae. They are closely crowded together, the reticular tissue of the tunica propria being reduced to a thin layer between the glands. Scattered fibers of smooth muscle from the muscularis mucosae may extend into the tunica propria. Three or more of these glands may open into a single gastric pit. Each gland consists of a short, narrow *neck*, which is followed by a longer and more expanded portion, the *body*, and a terminal blind end, known as the *fundus*. Occasionally the glands may divide into two or three branches, each of which ends in a slightly expanded fundus.

The gastric pits of the fundus and body of the stomach are wide and shallow. They are lined by a continuation of the epithelium which covers the gastric surface. An abrupt change in the epithelium occurs where it passes from the pits into the necks of the gland. The neck cells are low columnar with a clear cytoplasm and flattened, basally located nuclei. Like the cells of the cardiac glands, which they greatly resemble, they produce a modified mucoid secretion.

Two types of cells are present in the body of the gland: the *chief cells* and the *parietal cells*. The chief cells form the main cellular constituents of these glands. They border the lumen of the gland and in cross section are seen to be pyramidal in shape. Their cytoplasm is filled with numerous fine granules *(prozymogen granules)* from which the secretion of the cells *(pepsin)* is formed when the prozymogen is acted on by hydrochloric acid. Both the cytoplasm and the granules respond to the basic stains and, therefore, appear blue in sections. The spherical nucleus is located toward the basal portion of the cell. Basal striations are also present. The parietal cells may be either

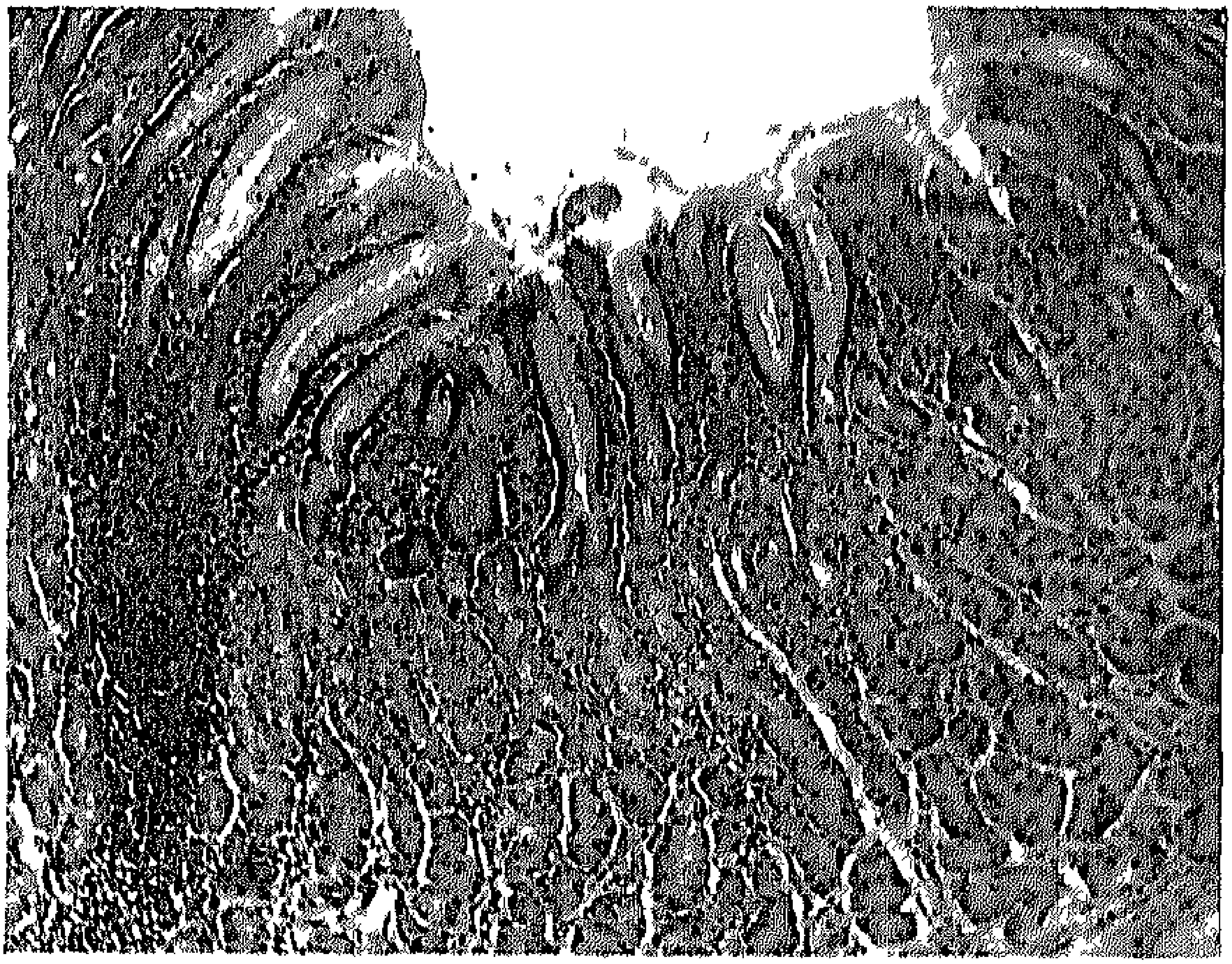


FIG. 129. Vertical section through the mucous membrane of the fundus of the stomach showing the gastric pits and simple tubular glands. Hematoxylin and eosin stain. Photomicrograph.

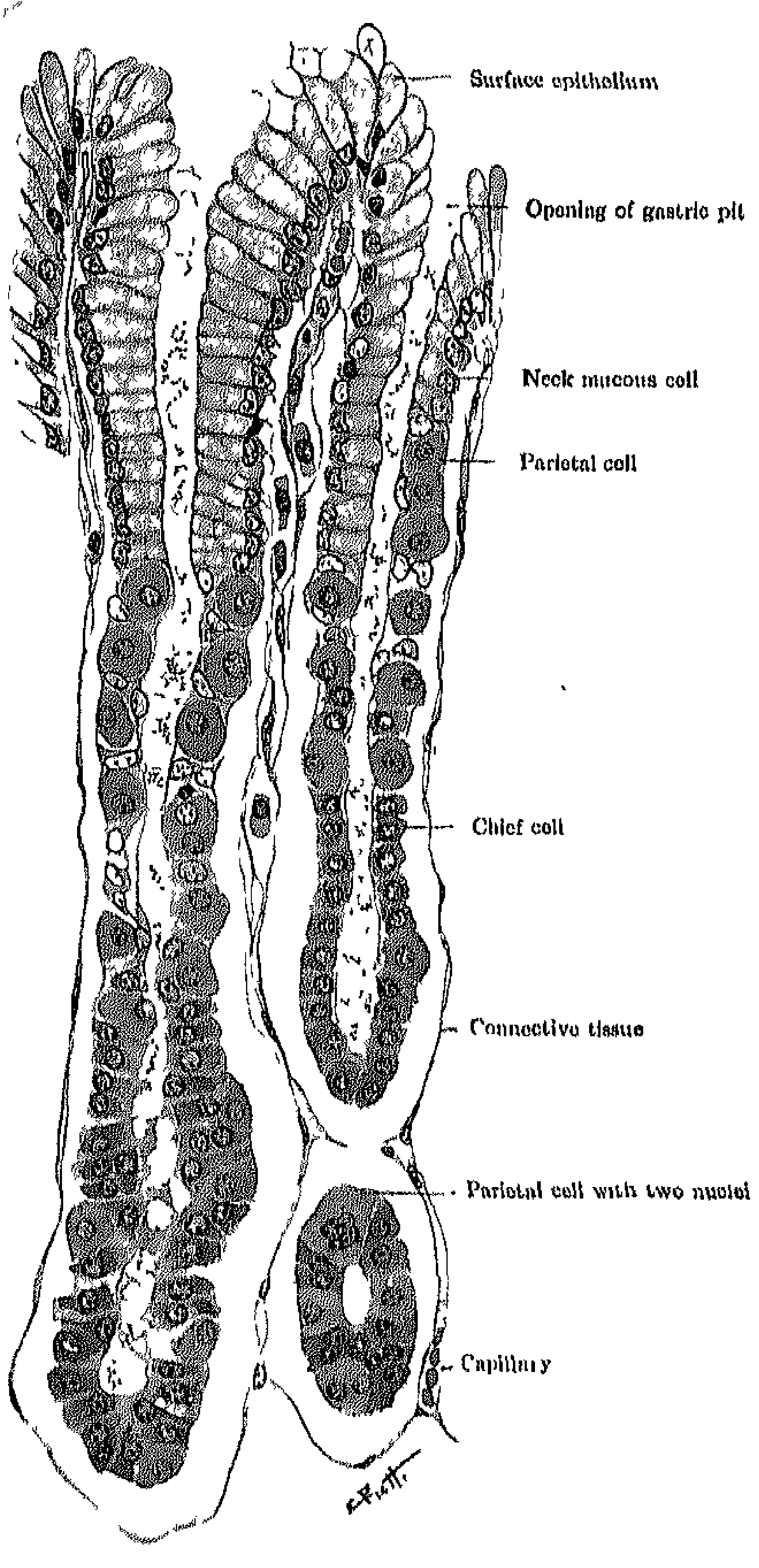


FIG. 180. A vertical section through the mucosa of a human stomach showing gastric pits and simple tubular gland. The parietal cells stain red, the chief cells blue and the mucous neck cells and surface cells a faint pink. Methylene blue and eosin stain. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

triangular, or almost spherical, in shape. They are not in contact with the lumen, but lie between the chief cells, their peripheral position causing the basement membrane to bulge outward. Their secretion reaches the lumen through intercellular canals which pass between the chief cells. The parietal cells are readily identified, in stained preparations, by their affinity for the acid stains, their red color contrasting sharply with the blue of the chief cells. The parietal cells are most numerous in the neck of the gland. They decrease in number toward the fundus, in which only a few of these cells may be found. Their function is believed to be the production of the substances from which the free hydrochloric acid of the gastric secretions is formed.

A few small cells occur among the chief cells which show an affinity for the silver stains, the *argentaffine cells*. These cells cannot be identified in ordinary preparations. Their function is unknown.

PYLORIC GLANDS. In the pylorus, the gastric pits are narrower and deeper than those in the body and fundus. They are lined by a continuation of the epithelium which covers the gastric mucosa. The glands, two or three of which open into a single pit, consist of a neck, which divides into a number of long tubular branches. The branches are somewhat longer than the neck and form the secreting portion of

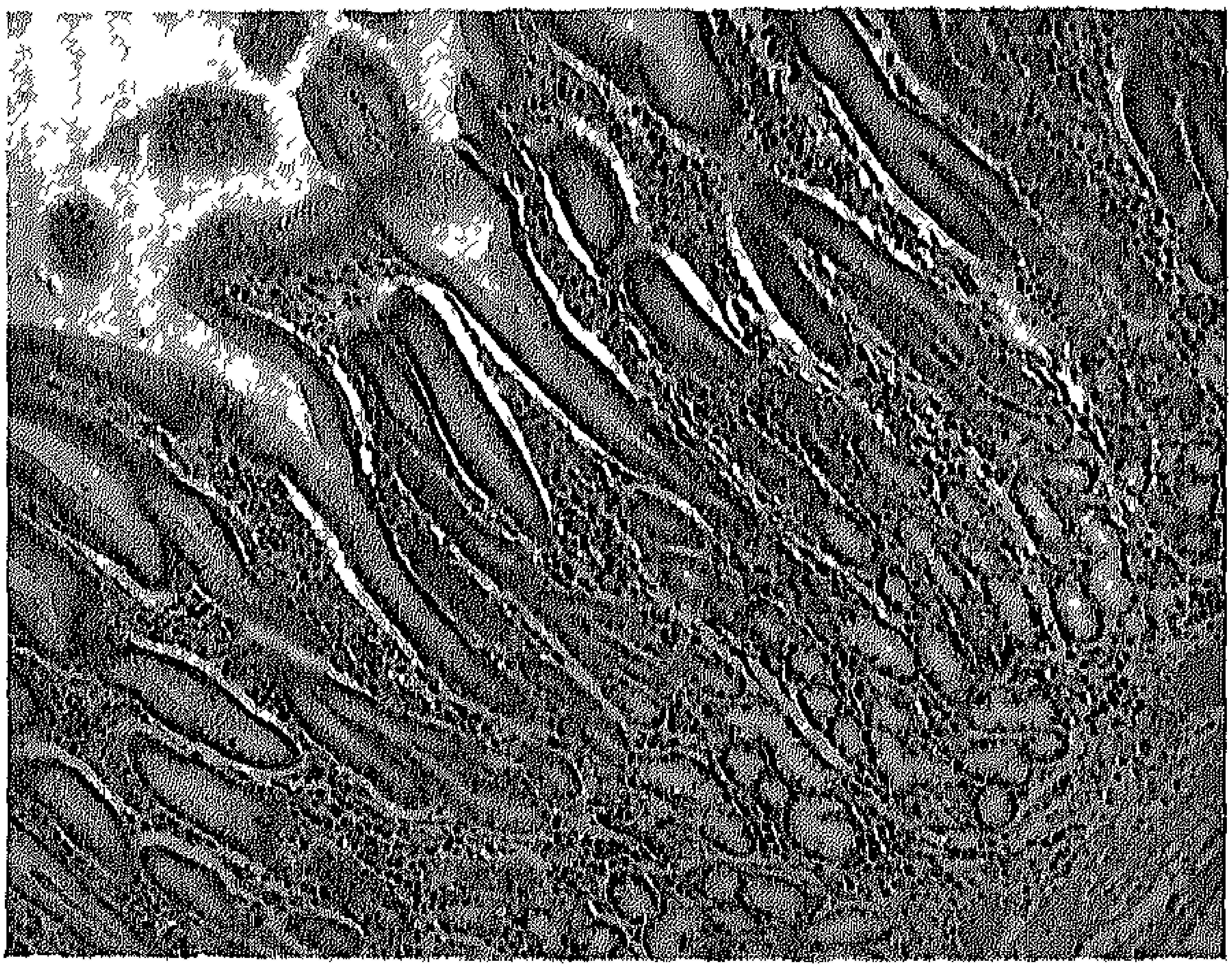


FIG. 181. Vertical section through the mucous membrane of the stomach (pylorus) showing the gastric pits and branched tubular glands. Hematoxylin and eosin stain. Photomicrograph.

the gland. They do not pass into the submucosa, but their terminal secreting portions lie close to the muscularis mucosae where they are seen, in sections, to be cut transversely and obliquely. The cells of the pyloric glands are similar to the neck cells of the gastric glands and, like them, produce a modified mucus secretion. As a rule parietal cells are not present, although occasionally they are found in the glands in the region of the pylorus. Smooth muscle fibers extend from the muscularis mucosae into the tunica propria and may be seen about the fundic and pyloric glands. By their contractions, these fibers aid the passage of the glandular secretions.

BLOOD AND LYMPH SUPPLY OF THE STOMACH. Branches of the *gastric* and *epiploic arteries* pass over the walls of the stomach in the connective tissue of the serous membrane. Their subdivisions pass into the gastric wall and break up into capillaries which supply the tissues of the muscular coat. Some of these branches continue into the submucosa where they unite to form a network of larger vessels, from which branches extend through the muscularis mucosae into the mucosa. These branches form a network (plexus) from which capillaries pass inward and surround the glands. The veins which arise from these capillaries assume plexiform arrangements both internal to the muscularis mucosae and in the submucosa. The larger veins which arise from these networks pass out of the gastric wall, generally following the course of the arteries.

The lymphatics arise from fine capillary networks about the glands and muscle fibers. They unite to form larger vessels, which pass from the wall of the stomach to empty into the lymph nodes in the adjacent connective tissue.

NERVE SUPPLY OF THE STOMACH. Groups of ganglion cells forming the *myenteric (Auerbach's) plexus* are located in the connective tissue septum between the circular and longitudinal layers of the muscular coat. Fibers from the ganglion cells are distributed to the muscle bundles of these layers, which they supply. Groups of similar cells, but much fewer in number, also occur in the submucosa *(submucous plexus: Meissner's plexus)*, their fibers supplying the tissue of the muscularis mucosae and epithelium. Parasympathetic fibers from the vagus nerves end in relation to the groups of ganglion cells. Fibers from the sympathetic division are also present, and end in the walls of the blood vessels. Myelinated fibers, probably sensory in function, break up into delicate fibrils which end between the cells of the gastric epithelium. Stimulation of the parasympathetic fibers cause the stomach musculature (except the sphincter muscle) to contract while the action of the sympathetic, when stimulated, is to inhibit contraction.

THE SMALL INTESTINE

The small intestine begins at the pylorus of the stomach and ends at the point where it joins the large intestine in the lower part of the abdominal cavity on the right side. It varies in length from 18 to 25 feet. In order to accommodate this length to the space which it occupies, the small intestine is arranged in a series of coils in the abdominal cavity. Three divisions of the small intestine are recognized: the *duodenum,* the *jejunum,* and the *ileum.* The duodenum is relatively short, being not more than 10 to 12 inches in length, while the jejunum constitutes two-fifths, and the ileum three-fifths of the remainder of its length.

The similarity of the general basic plan for the entire alimentary tract has already been mentioned, however, each segment has certain characteristics which identify it and these will be discussed.

Two structures are characteristic of the small intestine: the *plicae circulares (valvulae conniventes)* and the *villi.* The plicae circulares are permanent, shelflike folds, which are arranged in a circular manner about the inner wall of the intestinal canal, their extent being from one-half to two-thirds or more of its circumference. These folds serve to increase the absorption area and aid in churning the partially digested food. Obliquely directed folds, which extend from one transverse fold to another, are also present. The plicae vary in height in the different segments of the small intestine.

There are no plicae in the upper part of the duodenum. They reach their greatest development in the middle portion of the jejunum and gradually decrease in height in the lower part of the ileum. The plicae are formed by elevations of the submucosa which carry the muscularis mucosae and the mucosa with them. They should not be confused with the temporary, longitudinal folds which are present when the wall of the intestine is collapsed, but disappear when it is distended.

The villi are fingerlike projections of the mucous membrane, varying in number, height and shape in the different parts of the small intestine. They are most numerous and reach their greatest development in the duodenum and jejunum. They decrease in number and become progressively lower from the middle of the jejunum toward the end of the ileum. The villi in the duodenum are generally described as being leaf-shaped, they are tall and conical or rounded in the jejunum, and club-shaped in the ileum. On gross inspection their presence gives a velvety appearance to the surface of the mucosa.

The coats which make up the wall of the intestine are: *mucosa, muscularis mucosae, submucosa, muscularis externa* and the *serosa.*

The *mucosa* consists of the epithelial layer which rests on a thin

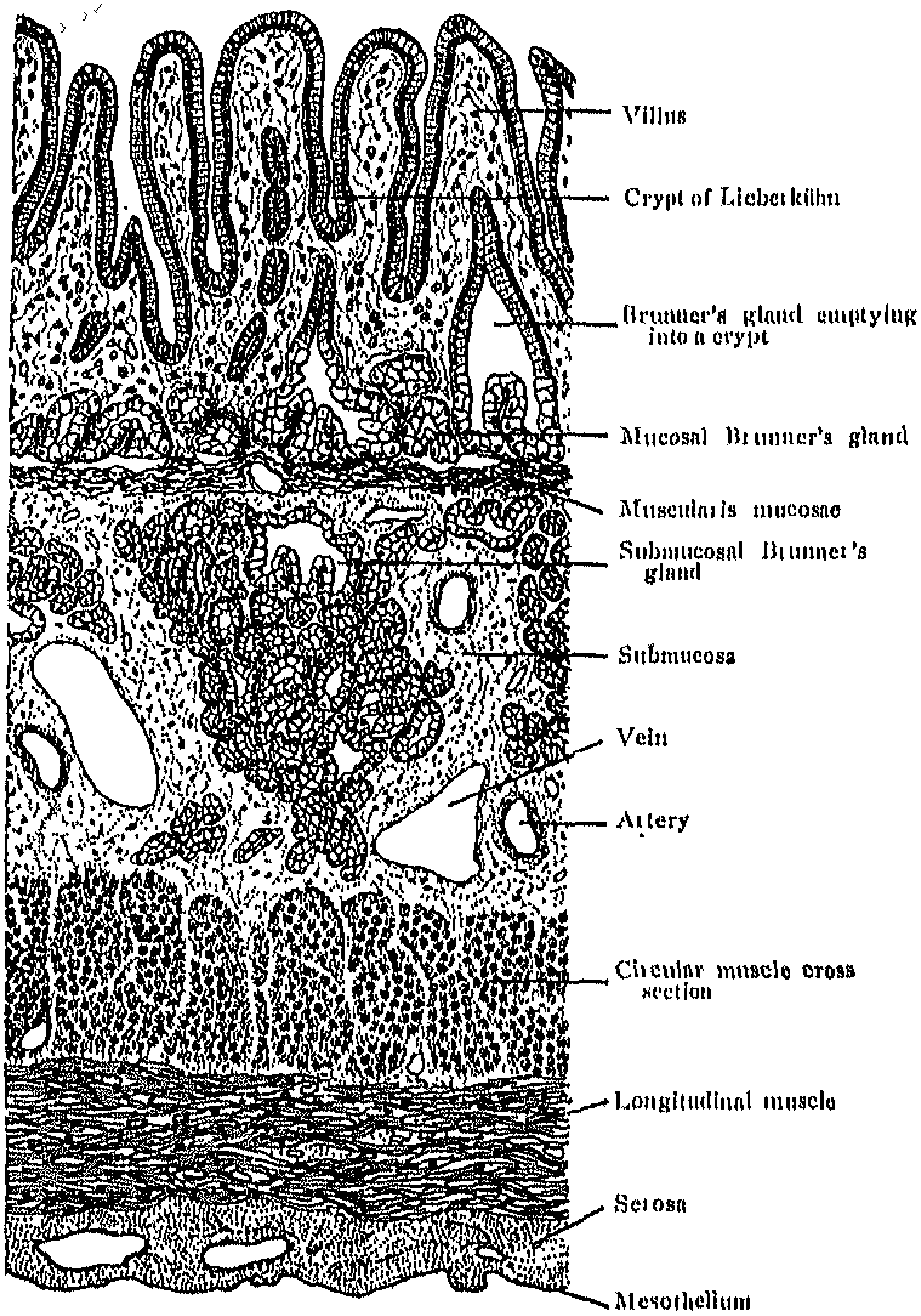


FIG. 132. Longitudinal section through the duodenum of man. 30 ×.

basement membrane, the tunica propria with variable numbers of lymphocytes, and glands. The small intestine can be identified by the presence of the villi.

Each villus consists of a *core* or supporting structure formed by the upward extension of tunica propria consisting of reticular connective tissue and lymphocytes. Besides the reticular cells and lymphocytes which are present in considerable numbers, plasma cells, mast cells and a few granulocytes are also present. These cells, especially the plasma and mast cells, are believed to be active in transferring the fat droplets from the epithelium to the lacteals. Resting upon this tissue is a continuation of the epithelium which covers the surface of the intestinal mucosa. The center of the villus contains a thin-walled lymphatic vessel, the *lacteal*, which starts as a blind saclike capillary. The lacteals receive the digested and absorbed fats, which give their contained lymph a milky appearance (*chyle*). When two or more lacteals are present in the villus, they are joined to one another by delicate endothelial tubes or branches. However, the lacteals are not seen in most histological specimens because they collapse on fixation. Smooth muscle fibers extending into the tunica propria from the muscularis mucosae are located along the sides of the lacteals and by their contractions they aid the passage of the chyle. The blood capillaries, which are in the form of loops, lie close to the inner surface of the epithelium. Both the plicae circularis and the villi increase the surface area of the intestine which is used for absorption.

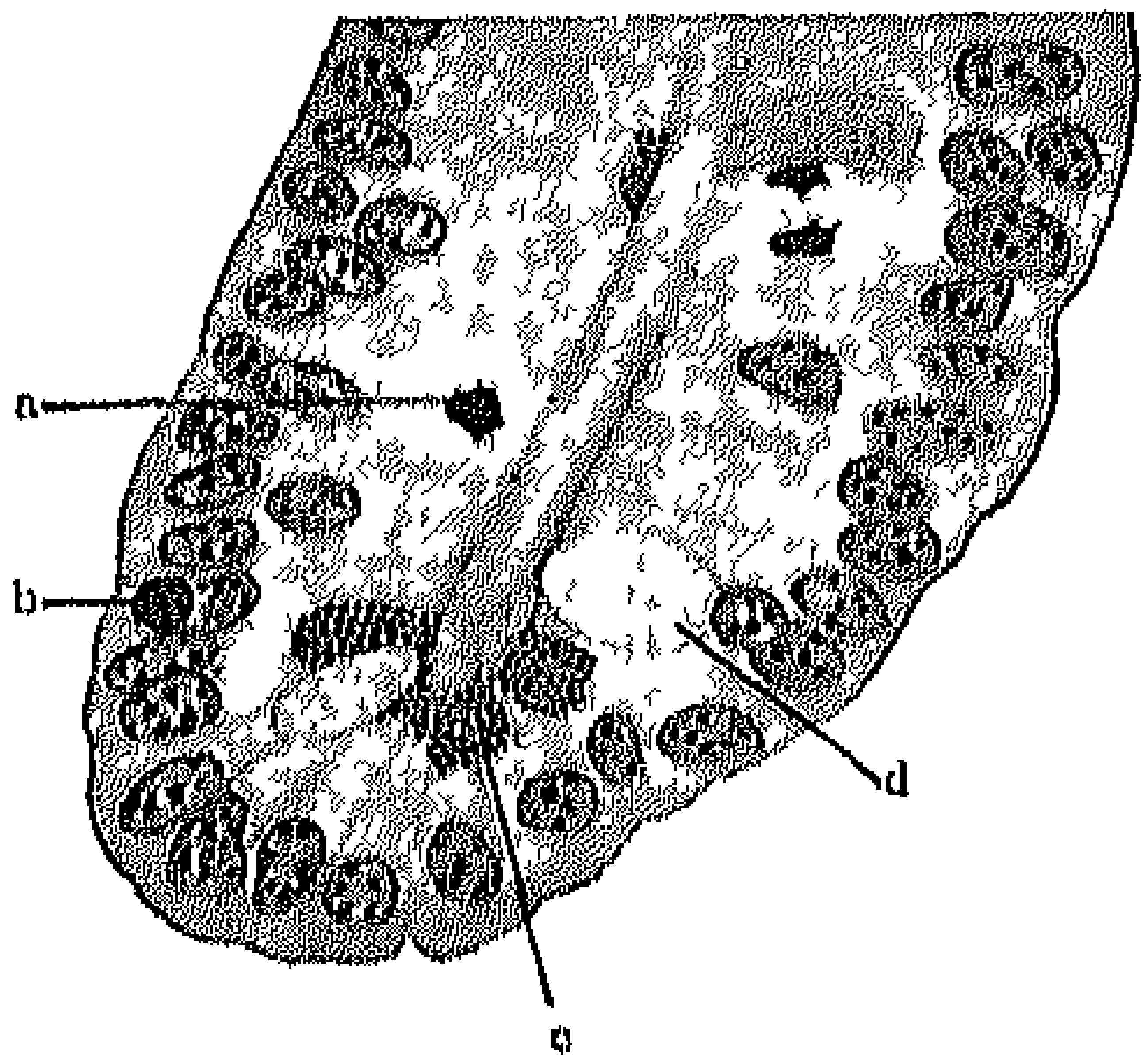


FIG. 133. The fundus of an intestinal gland from the duodenum of a guinea-pig. 480 ×. (a) Cell in mitosis. (b) Lymphocyte. (c) Paneth's cell. (d) Goblet cell.

Small, porelike openings are found in the epithelium between the bases of the villi, which lead into the simple tubular or *intestinal glands* known as the *crypts of Lieberkühn*.

Lymphocytes are scattered throughout the mucosa of the intestine. They are also present in the form of diffuse aggregations and as nodules. The nodules may appear singly (*solitary nodules*), or in groups (*aggregated follicles; agminated glands*), when they are commonly referred to as *Peyer's patches*.

In all, the epithelium of the small intestine contains five different cell types, one of which is limited to the surface, one is found in both the surface epithelium and the epithelium lining the crypts, while the remaining three are found in the crypts.

The epithelium which forms the immediate lining of the small intestine is composed of simple columnar cells, whose basal processes are interwoven with a thin layer of delicate fibers from the underlying reticular tissue. These fibers are condensed to form the basement membrane on which the epithelium rests. Two types of cells contribute to the formation of the surface epithelial layer. Most numerous are the tall columnar cells, whose chief function is absorption. Intermingled with these cells are a considerable number of goblet cells. These cells are relatively few in the upper part of the small intestine, but are more numerous toward its lower end.

The *columnar absorbing cells* have a finely granular cytoplasm. The nuclei are oval and located toward the basal portion of the cell. Mitochondria and Golgi apparatus are both present and attempts have been made to associate the latter with the absorption of fats. These cells are provided with striated cuticular borders.

A considerable number of *goblet cells* appear as broadly oval, clear spaces in the epithelium. These cells, which secrete a mucoid substance, are most abundant in that portion of the epithelium which extends over the villi. Goblet cells are so-called because of their fancied resemblance to a drinking glass or goblet. They differ from the other cells of the epithelium, not only in their ability to produce a mucoid secretion, but also in the form and staining quality of their nuclei. After the mucoid substance has been expelled, the cytoplasm increases in amount and fills the body of the cell which, at this stage, is not unlike the other cells of the epithelium. They can be identified, however, by the absence of the cuticular membrane and by a densely stained nucleus. Droplets of mucoid material form in the cytoplasm. These droplets coalesce into the homogeneous, mucous substance which distends the cell and causes it to assume the gobletlike appearance. As the mucoid substance increases in the cell, the cytoplasm containing the nucleus is pressed into the narrow, stemlike base of the cell. During the early stages in its development, the mucoid substance has a strong affinity for the basic stain. In this stage, goblet cells have the appearance of dark oval bodies located among the cells of the epithelium.

The crypts of Lieberkühn are simple tubular glands which extend downward in the tunica propria as far as the muscularis mucosae. These glands are not set as closely together as the gastric glands, for which reason a considerably greater amount of reticular tissue may be seen between them. The epithelium lining the crypts contains several types of cells: *undifferentiated columnar cells, goblet cells, Paneth cells* and *argentaffine cells (chromaffin cells).* The cells of the intestinal epithelium undergo a transition as they pass into the upper part, or neck, of the crypts, where they become considerably lower. These cells have a less well-defined cuticular border than the surface cells. Cells located near the middle part of the gland show numerous mitotic figures. These cells give rise possibly to either the columnar absorbing cells or the goblet cell. The cells in the lower end or fundus of the gland are pyramidal in outline and are somewhat larger and lower than the cells in the neck. They represent the undifferentiated columnar cell. They have no cuticular border.

The cells of the intestinal epithelium undergo degenerative changes and are cast off. They are replaced by cells which are formed in the neck region and sometimes in the fundi of the crypts. The cells of the epithelium are pushed upward as the new cells are formed beneath them.

Goblet cells are found throughout the crypt, but are most numerous in the upper part. They are typically mucus-secreting cells and have been adequately described elsewhere.

A number of large cells located in the fundi are to be distinguished by their large, oval nuclei and the coarse, highly refractive granules with which their cytoplasm is filled. They are known as the *cells of Paneth.* These cells have been shown to possess a definite secretory function. Since the granules disappear from the cell during digestion and are reformed during fasting, it is believed this secretion is concerned with the digestive process. However, the nature of the secretion produced by the Paneth cells is unknown.

Small cells which occur among the epithelial cells of the crypts and which may also be found among those over the villi are known as *argentaffine cells* because of their affinity for silver stains. These cells were formerly called *chromaffin cells* because of their capacity for retaining the brownish yellow color produced by the application of the salts of chromic acid. They are thought to have a secretory function, but little is known concerning their function.

The tunica propria lies beneath the epithelial layer and extends into the villi and between the glands. It rests on the muscularis mucosae and consists primarily of reticular connective tissue and lymphocytes. Scattered collagenous and elastic fibers may be found. In the tunica propria of the intestinal wall the lymphocytes are abundant. Wherever considerable aggregations of lymphoid tissue are present in the wall of the intestine, lymphocytes may be seen pushing their way between the cells of the epithelium to reach its surface. The number of lymphocytes may be so great in some areas, that the epithelium has the appearance of being obliterated. Besides the lymphocytes, plasma cells and mast cells may be present in considerable numbers in the reticular tissue of the tunica propria. Granular leucocytes are also present, and of these, the eosinophils are the most numerous. The lymphocytes are generally scattered diffusely throughout the layer but, here and there, the lymphoid tissue is organized in the form of scattered nodules known as *solitary nodules*. These nodules are oval in shape and are usually confined to the tunica propria, however, they may invade the muscularis mucosae and enter the submucosal area where they form large nodules. In the region of the ileum the lymphoid tissue becomes very profuse and instead of single (solitary) nodules, there are a number of these nodules joined together in an aggregate form. For this reason they are referred to as *aggregated follicles* and are known as *Peyer's patches*. If the ileum is split longitudinally and laid open, the areas occupied by Peyer's patches may be recognized grossly as elongated, oval areas extending lengthwise of the ileum on the wall opposite the attachment of the mesentery. Microscopically, these areas are seen to consist of a variable number of nodules arranged side by side. No villi appear over the area of a Peyer's patch, but the columnar epithelium extends across the area and separates it from the lumen of the intestine. These patches are usually confined to the tunica propria, but may extend into the submucosa. The number of follicles making up the Peyer's patches vary considerably. They may consist of as few as 8–10 and they may have as many as 60–70 separate follicles.

The *muscularis mucosae* consists of smooth muscle bundles arranged for the most part in an inner circular and an outer longitudinal layer.

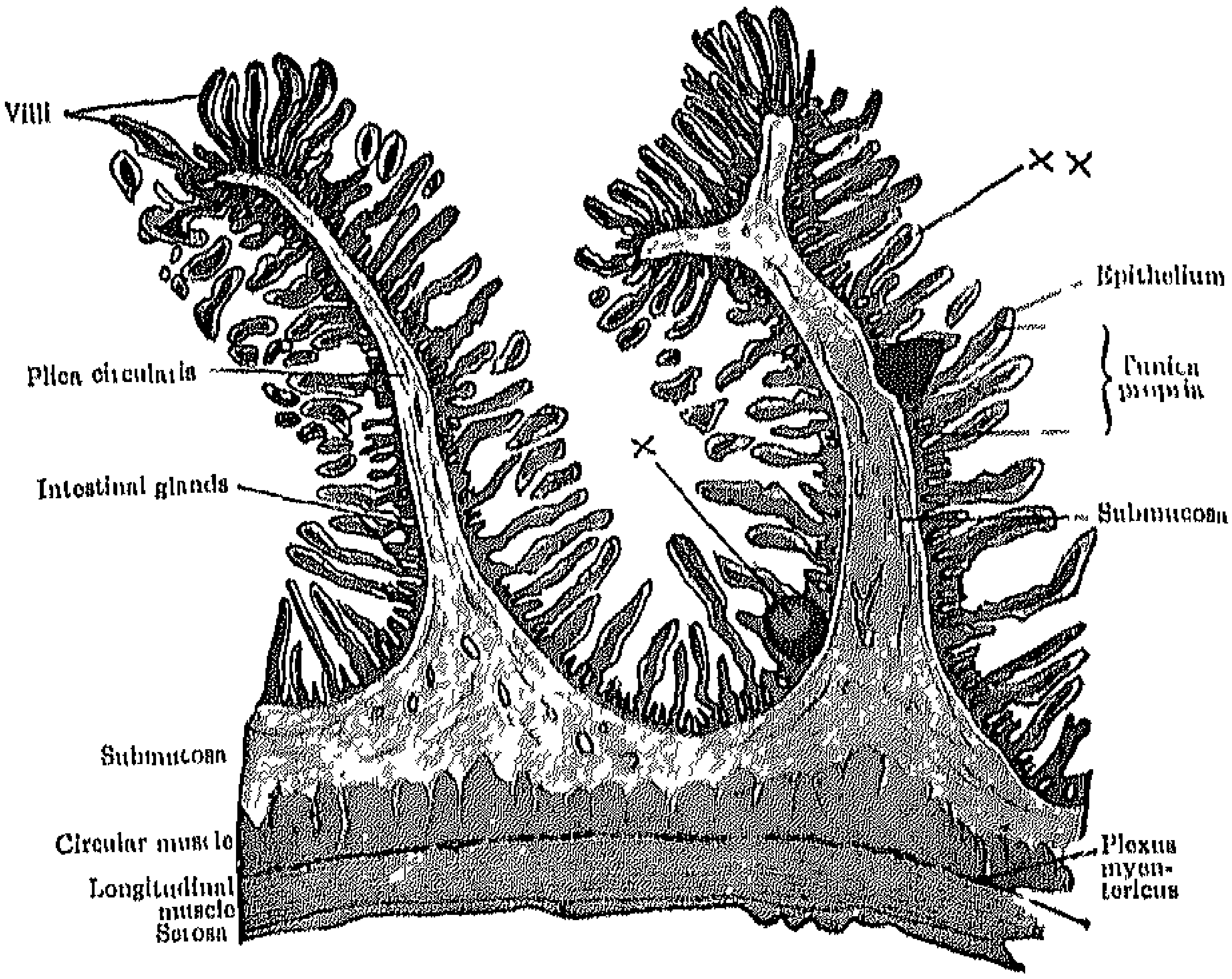
The *submucosa* in the small intestine, as elsewhere throughout the digestive tract, consists of loosely arranged collagenous and elastic fibers and contains blood and lymph vessels, nerves and the ganglion cells of Meissner's plexus. Glands are found in this layer only in the upper part of the duodenum. They are the *duodenal glands* or more commonly called *Brunner's glands*. These glands are branched tubular in type and their ducts either empty into the base of a crypt or they may empty directly into the base of an intervillus space. Both the secreting end pieces and the ducts are lined by a simple columnar epithelium. The glands are occasionally absent.

The *muscularis externa* consists of a relatively wide area of smooth muscle bundles arranged in an inner circular and an outer longitudinal layer. The muscle is enclosed in a connective tissue layer which sends septa between the muscle bundles and also forms a well defined layer separating the circular and longitudinal layers. In this intermuscular layer lie the ganglion cells of Auerbach's plexus.

The *serous coat* is thin and consists of loosely arranged connective tissue with an outer layer of mesothelial cells.

The blood and nerve supply of the small intestine corresponds to that which has been described for the alimentary tract.

The special characteristics of each segment will now be discussed briefly by way of summarizing the above material.



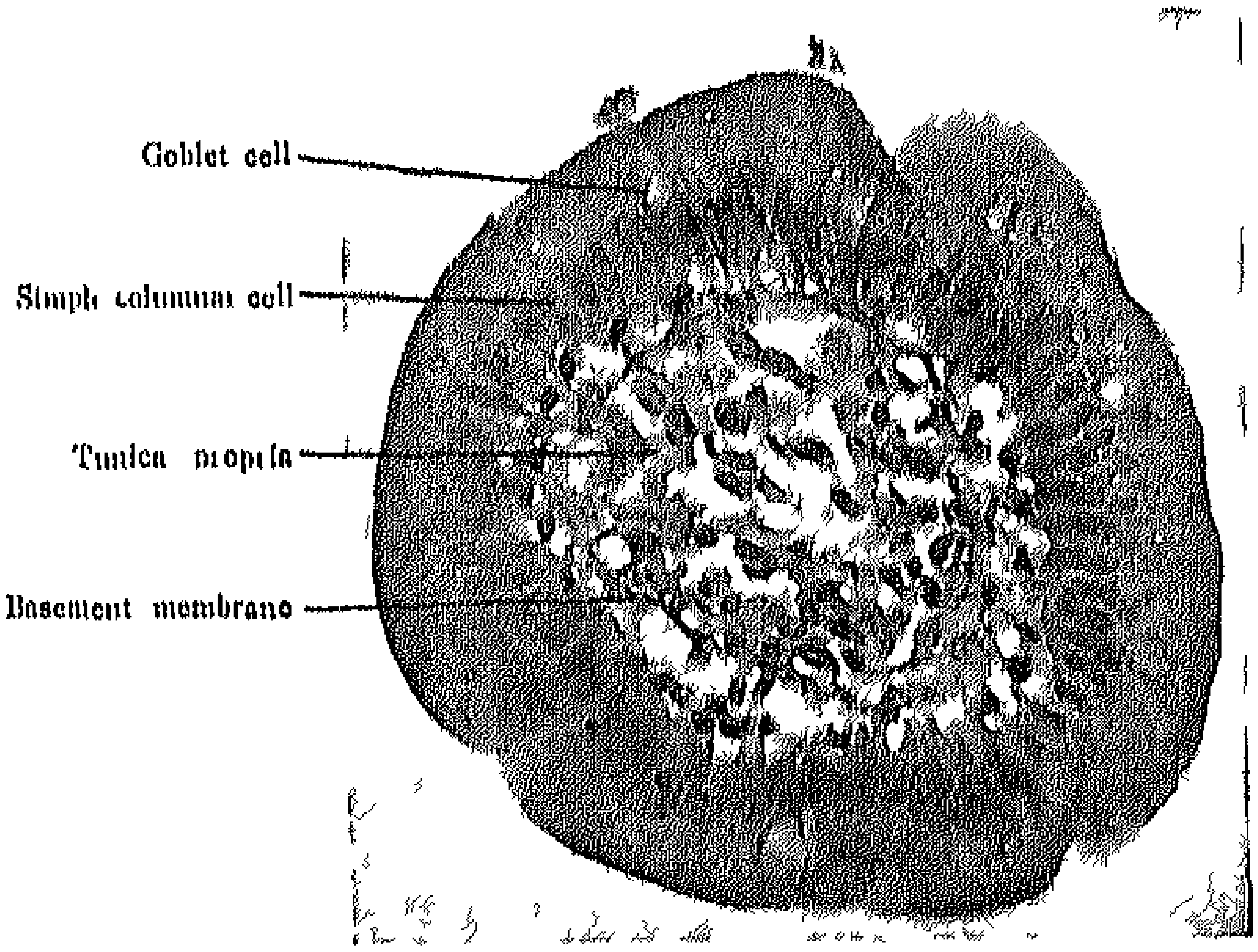


Fig. 134. *(Top)* Vertical longitudinal section of the jejunum of an adult man. 16 × The plica circularis on the right supports two small solitary nodules which do not extend into the submucosa. One of them exhibits a germinal center ×. The epithelium is slightly loosened from the connective tissue core of many of the villi so that a clear space, ××, exists between the two. The isolated bodies lying near the villi (more numerous to the left of the plicae circulares) are sections of villi that were bent so that their ends were cut off in sectioning. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

Fig. 135 *(Bottom)* Cross section of a villus from human jejunum. Photomicrograph.

THE DUODENUM

The wall of the duodenum is somewhat thicker than that of the other portions of the small intestine. Its epithelium consists of tall, columnar cells, among which goblet cells are present, especially in that portion which is carried over the villi. The plicae circulares are low and broad where they first appear near the middle portion of the duodenum, becoming taller and narrower toward its lower end. The villi are broad and leaflike.

Two types of glands are present: the *crypts of Lieberkühn* and the *glands of Brunner.* The crypts are simple tubular invaginations of the epithelium which extend only as far as the muscularis mucosae. The crypts are present throughout the length of the duodenum. Brunner's glands are branched tubular structures located principally in the submucosa, in which their coiled tubules form considerable masses of glandular tissue. These glands are most numerous between the pylorus and the ampulla of Vater, becoming less frequent until they disappear from the wall of the duodenum before its lower end is reached. Occasionally they may be absent. Their presence is diagnostic of duodenum, but a section may be seen in which no Brunner's glands occur.

Near its middle part the wall of the duodenum is penetrated by the combined bile and pancreatic ducts (or the ducts may enter separately), which communicate with its lumen through an opening at the summit of a moundlike elevation, the *biliary caruncle* or *ampulla of Vater.*

THE JEJUNUM

The wall of the jejunum is somewhat thinner, and owing to a richer blood supply, is considerably darker (in fresh tissue specimens) than that of the duodenum or the ileum. The plicae circulares reach their greatest development in the jejunum where they are tall, thin structures with secondary and tertiary folds which, in sections, give them the appearance of being branched.

The mucosa is a relatively thin layer. It contains the crypts of Lieberkühn, which are similar to those found in the duodenum, with the exception that they are much shorter, their length being conditioned by the depth of the mucosa. The villi are tall and conical in the jejunum. Goblet cells are present in the epithelium covering the villi and a few of these cells

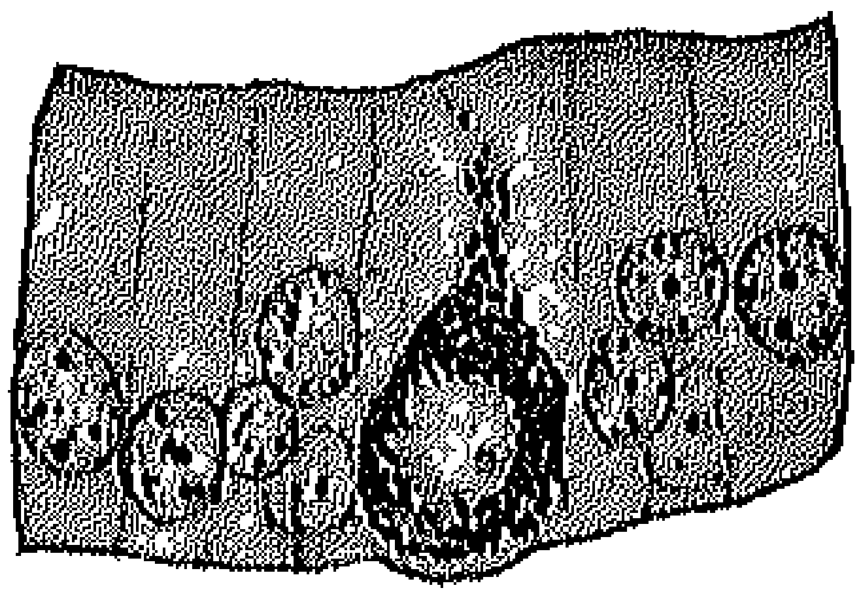


FIG. 136. A section of epithelium from the small intestine of a rabbit showing an argentaffin cell. Formaldehyde fixation Bodian impregnation. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

may also be found in the epithelium of the upper portions of the crypts. Lymphoid tissue is present in the tunica propria in the form of numerous lymphocytes scattered throughout its reticulum. It also occurs in the form of diffuse aggregations and as solitary nodules, which become very common in the middle part of the jejunum.

The Ileum

The plicae circulares become lower and less complicated in the ileum. They seldom show secondary or tertiary folds. The villi are smaller and fewer in number in the ileum as compared with the jejunum. They are generally described as being club-shaped. Aggregations of lymph nodules, known as *Peyer's patches (agminated glands; aggregated follicles)*, are found in the lower half of the ileum. They occur in that portion of the intestinal wall which is opposite the attachment of the mesentery. A Peyer's patch consists of a number of pear-shaped lymph nodules most of which show well-developed germinal centers. Their narrow portions are located in the tunica propria, their enlarged portions break through the muscularis mucosae and occupy a considerable part of the submucosa. The tissue between the nodules is occupied by a diffuse mass of lymphocytes. Both crypts of Lieberkühn

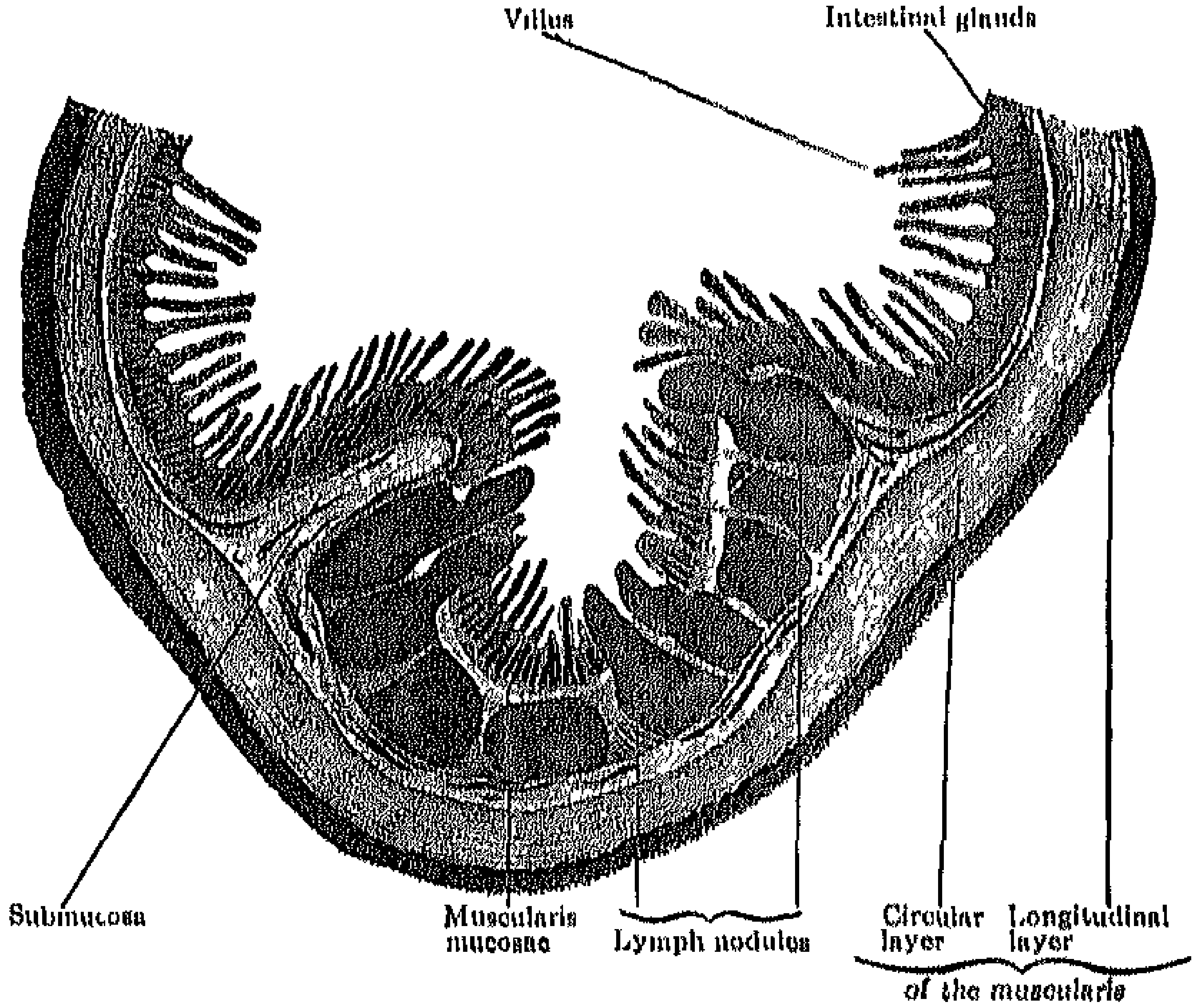
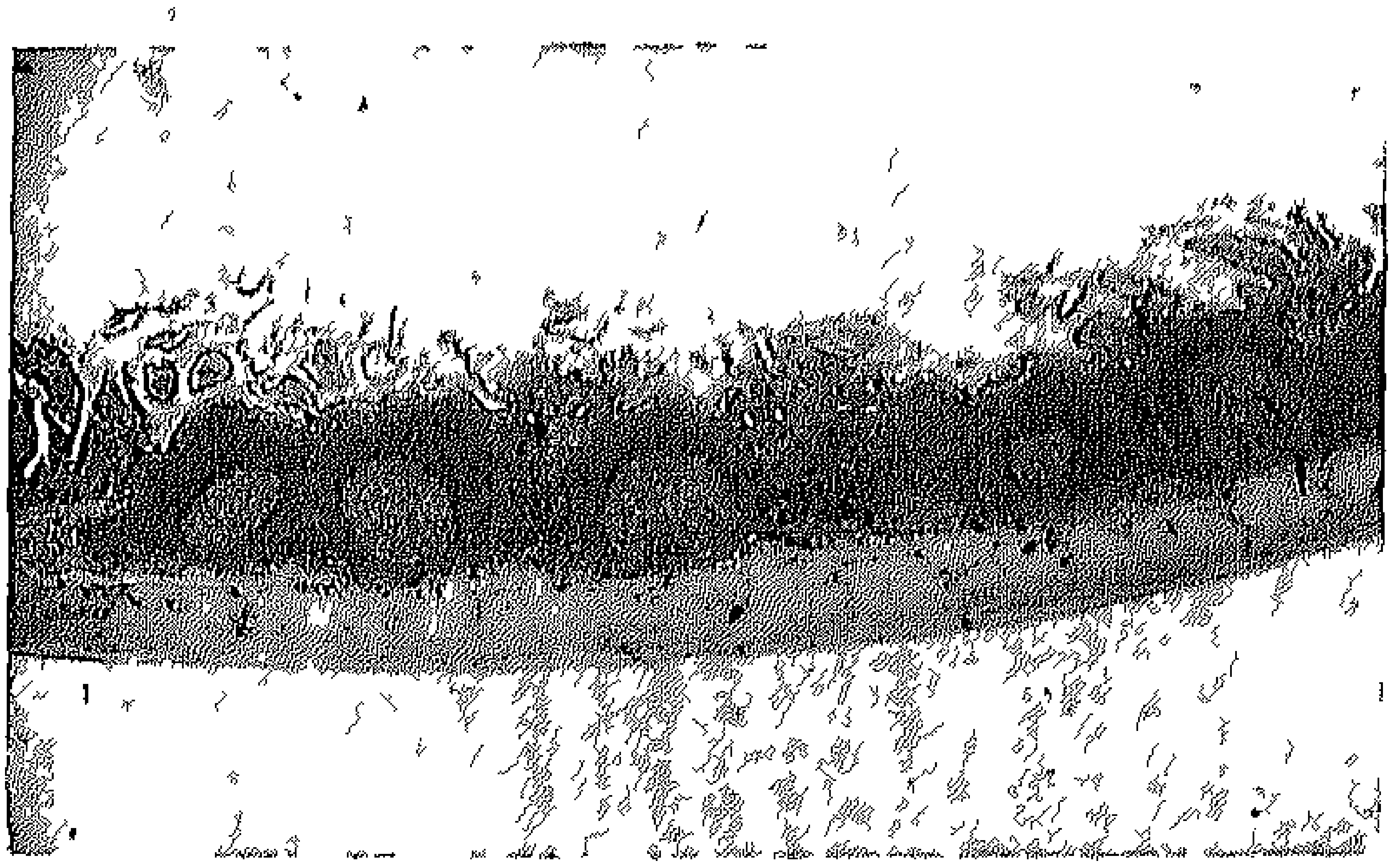


FIG. 137. Transverse section of aggregate nodules of the small intestine of a cat. The crests of four nodules were not within the plane of the section. 10 × (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)



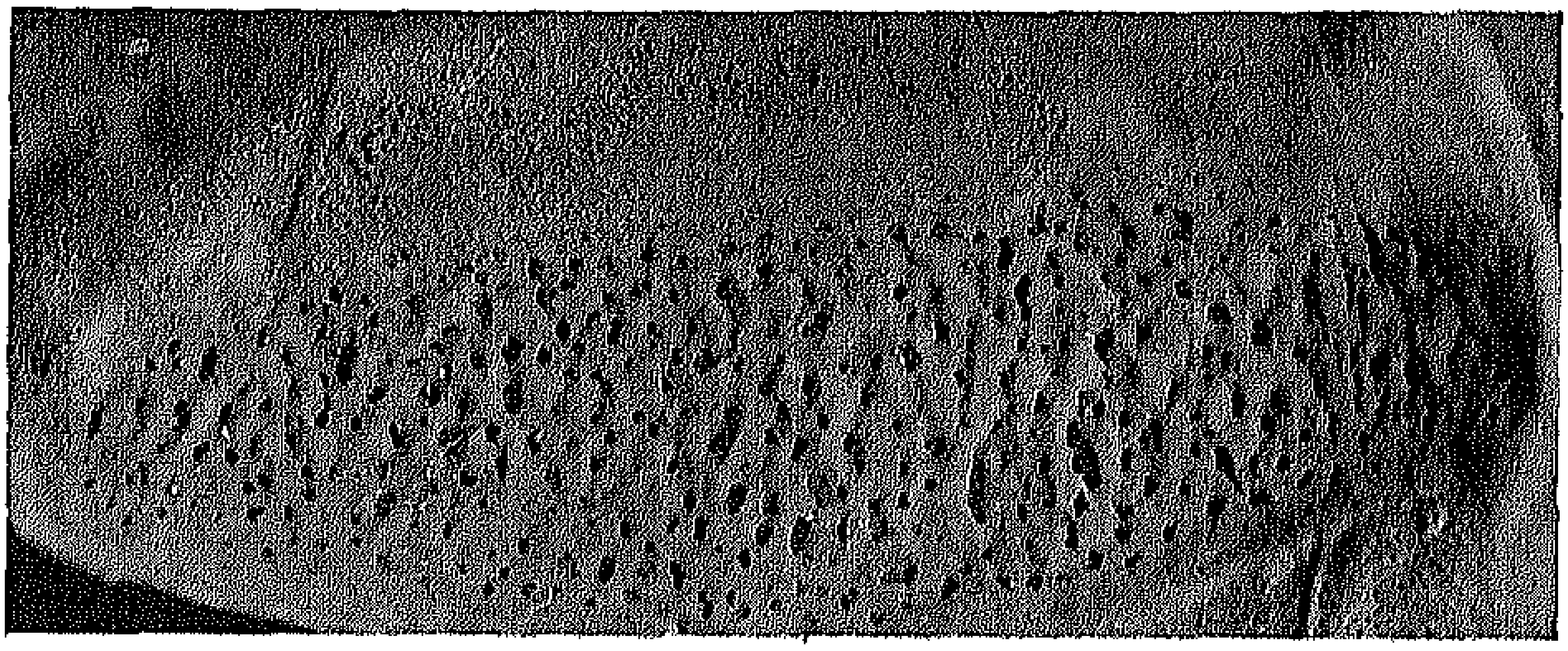


FIG. 138. *(Top)* Peyer's patch (human). Photomicrograph.

FIG. 139 *(Bottom)* Portions of ileum to show a Peyer's patch and solitary lymph nodules as they appear on gross examination Enlarged.

and villi are absent from the region above a Peyer's patch, but broken portions of the muscularis mucosae may be seen between the nodules. In the lower end of the ileum, the lymphocytes are found in the form of diffuse aggregations or solitary nodules.

THE ILEO-COLIC (ILEO-CAECAL) VALVE

The walls of both the small and large intestines join to form two lips, one above the other, bounding the slitlike aperture through which the contents of the ileum pass into the large intestine *(colon)*. These lips form a valvelike structure *(ileo-colic valve)*, the closure of which prevents the intestinal residue, once it has been received by the colon, from passing back into the ileum.

The mucosa on the sides of the lip of the valve which oppose each

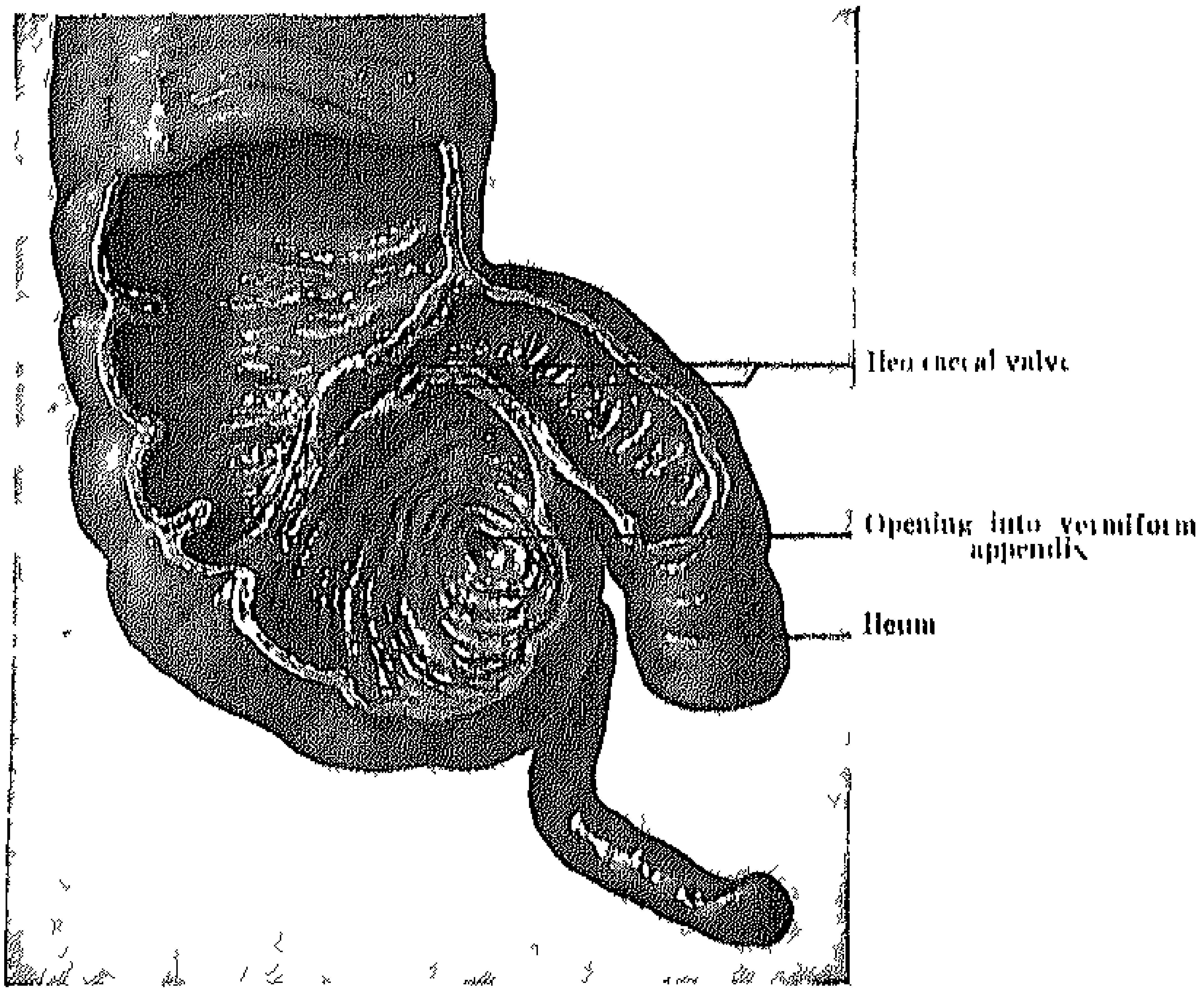


FIG. 140. Ileo-caecal valve and neighboring segments of intestine viewed from in front.

other, belongs to the ileum and is characteristic of it. It forms a relatively thick layer and contains crypts of Lieberkühn, low, conical villi, aggregations of lymph nodules and a muscularis mucosae. The mucosa on the side of the valve lips toward a caecum has no villi, but is supplied with wide crypts of Lieberkühn (the structure is similar to that of the colon), the epithelium of which contains numerous goblet cells.

The muscularis mucosae and submucosa of the ileum pass over the border of the lip and become continuous with the same coats of the colon *(caecum).*

In the muscularis externa, the inner circular layer of smooth muscle fibers extends into the lips of the valve where it forms a small sphincter muscle which aids in the closure of the valve. The outer longitudinal muscular layer also extends into the lips of the valve where it joins the corresponding layer from the colon.

THE LARGE INTESTINE

The large intestine, or *colon,* begins in the lower portion of the abdominal cavity on the right side. Its first division, the *ascending colon,* extends upward to a point below the liver where it turns to the left, passing in front of, and a little below, the stomach as the *transverse colon.* It makes another turn in the region of the spleen, and passes downward on the left side as the *descending colon.* At the level of the pelvic brim it passes toward the median line of the body, forming an S-shaped curve for which reason it is known as the *sigmoid colon*. The sigmoid colon ends in an expanded tube, the *rectum*. The lower end of the ascending colon forms a blind sac, which extends for an inch or more below the point where it is joined by the small intestine. This is known as the *caecum*. On the median side of the colon, near its junction with the ileum, a narrow tubelike structure of variable length, the *appendix*, is attached.

The large intestine also has a wall consisting of several coats: *mucosa, muscularis mucosae, submucosa, muscularis externa* and *serosa*, similar to those throughout the other segments of the digestive tract.

The *mucous membrane* of the colon differs from that of the small

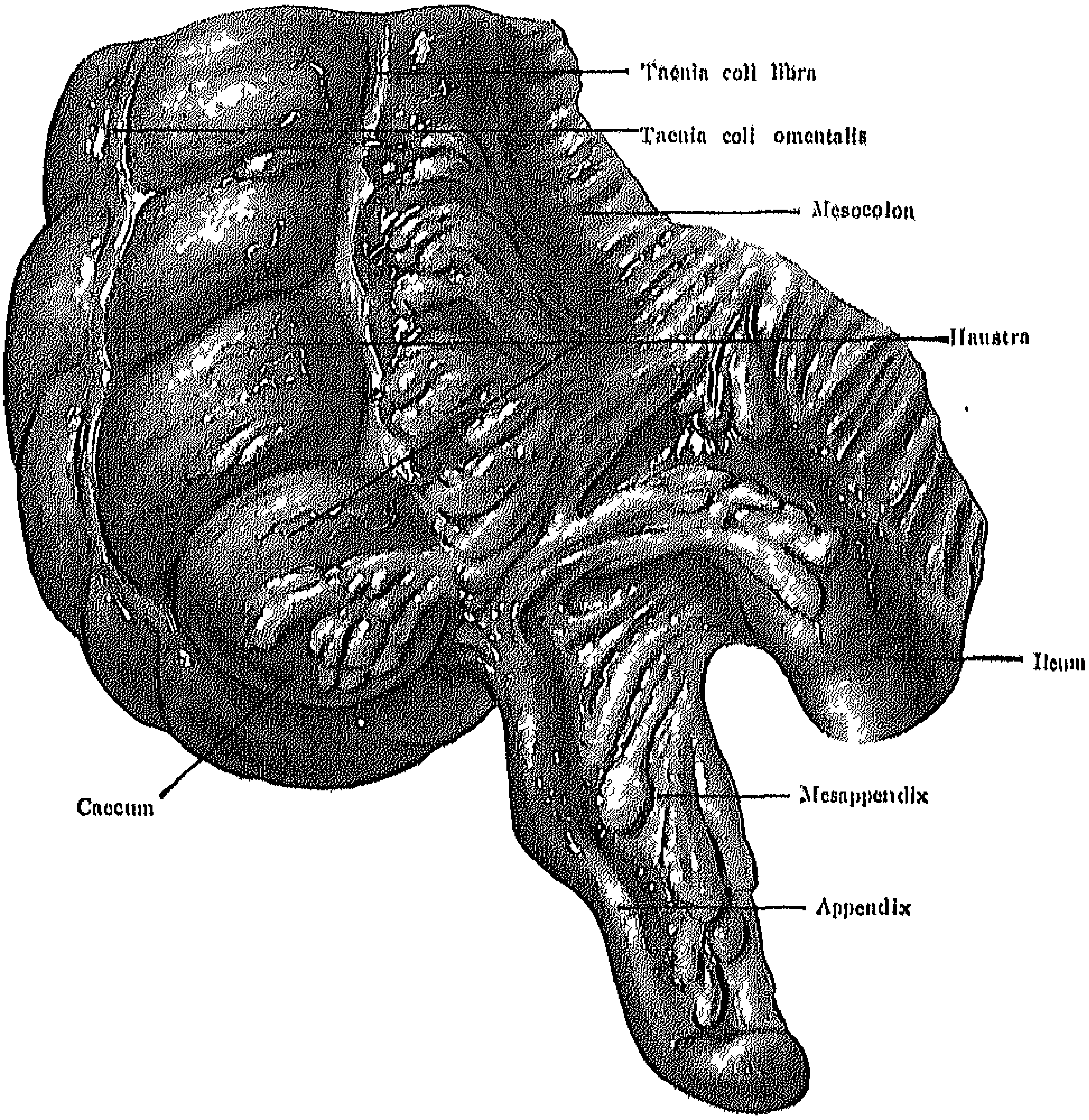


FIG. 141. Caecum and portion of ascending coli to show taenia coli and haustra.

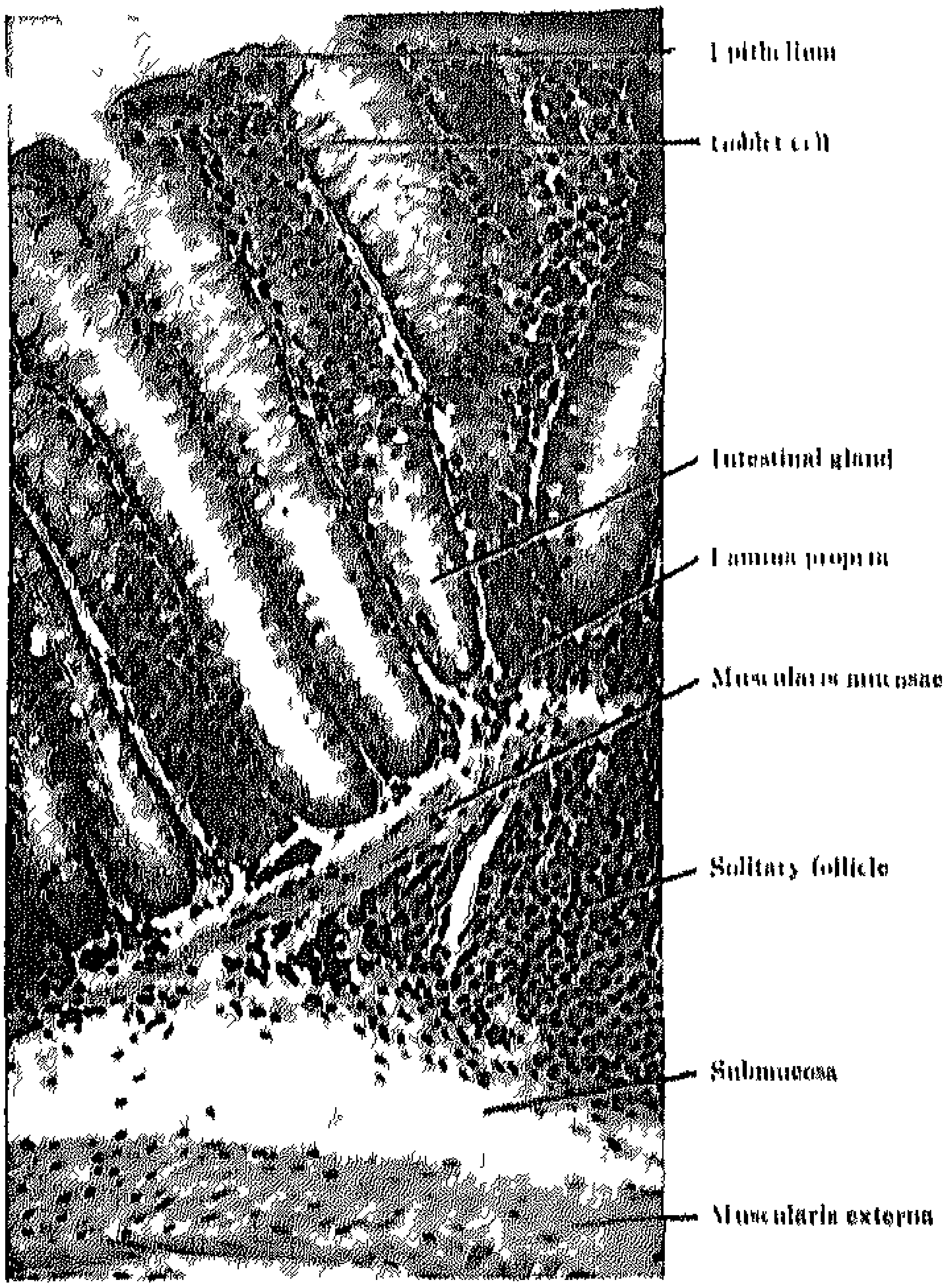


FIG. 142. Mucosa from the colon. (Courtesy, Snell: "Biology of the Laboratory Mouse," Philadelphia, The Blakiston Company.)

intestine in the complete absence of villi and plicae. The surface of the mucosa is, therefore, relatively smooth. This smooth surface is interrupted by numerous small openings which represent the openings of the simple tubular glands (crypts of Lieberkühn) which are found in the mucosa. The epithelium of the mucosa consists of simple columnar cells. These cells are tall and have a narrow striated cuticular border. The cells decrease in height as they enter the crypts, and in the fundus of the gland appear as undifferentiated cells as previously described. Numerous goblet cells are present in the epithelium in the crypts. The goblet cells are usually confined to the upper two-thirds of the crypts, although a few may be found among the cells of the fundus. As a rule they are not found among the cells of the epithelium on the surface. Argentaffine cells, and occasionally the cells of Paneth, are found in the crypts. Solitary nodules occur in the mucosa in which they lie close to the muscularis mucosae, and through which they frequently break to occupy a portion of the submucosa. The function of the epithelium of the large intestine is to absorb water, salts and glucose, thereby gradually reducing the intestinal contents to a semi-solid mass, the *feces,* and the production of large quantities of mucus for the purpose of lubricating the intestinal wall, as a means of aiding the downward passage of the fecal mass.

The *muscularis mucosae* is identical to that in the small intestine. It is composed of two layers of smooth muscle, the inner layer of circularly directed fibers and the outer layer of longitudinally arranged bundles.

The *submucosa* consists of interwoven bundles of connective tissue in which there may be fat cells.

The *muscularis externa* consists of two layers of smooth muscle fibers. The circular layer is strongly developed and forms a continuous layer. The fibers of the outer longitudinal layer are gathered into three thick bands, the *taeniae coli.* The longitudinal fibers between the taeniae are reduced to a thin layer or in rare instances they may be absent altogether.

The taeniae are shorter than the remainder of the wall of the colon which is attached to these bands by being gathered into a number of saclike folds, the *haustra.* This folding of the wall results in the formation of transverse ridges on the inner surface where the haustra are attached to the taeniae. These ridges, which extend into the lumen of the colon, include not only the mucosa and submucosa, but a part of the muscular coats as well. They are known as *plicae semilunares.*

The *serous coat,* where it is attached to the wall of the colon, is extended in the form of a series of pouchlike structures, the *appendices epiploicae.* They occur in considerable numbers on the wall of the transverse colon. They are not as numerous on the ascending and descending divisions, and appear only occasionally on the sigmoid colon. The *epiploic appendices* contain a large amount of adipose tissue, blood vessels and frequently, a large lymph node.

THE VERMIFORM APPENDIX

The vermiform appendix is a tubular outgrowth from the caecum. It varies from less than an inch to two or more inches in length. Its average diameter is about that of a common lead pencil. It extends into the abdominal cavity below the point where the small intestine joins the colon. It is supported by a mesentery, the *mesoappendix,* in which blood vessels and nerves pass to its walls.

The vermiform appendix in younger persons has a distinct lumen

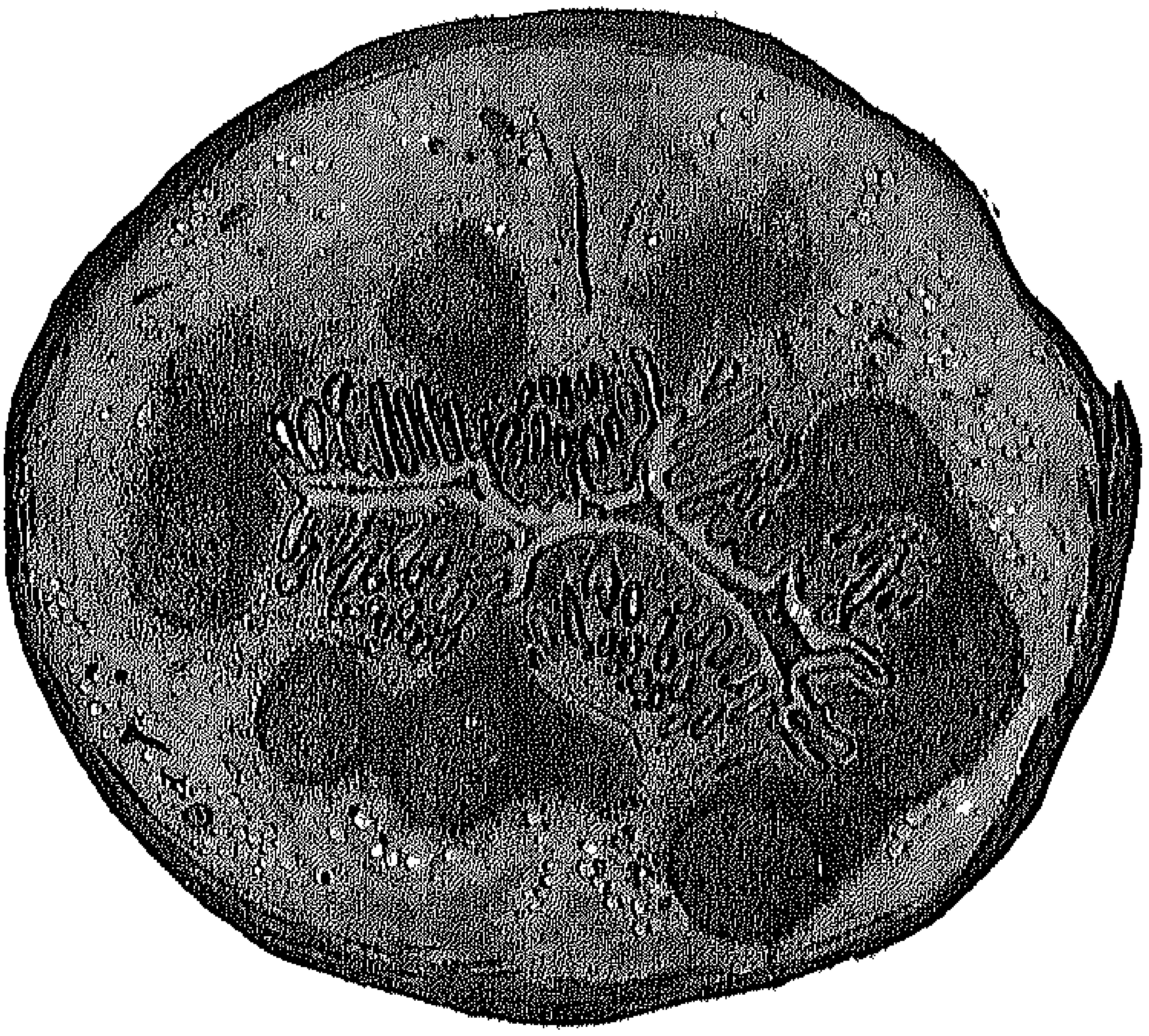


Fig. 148. Cross section of a human appendix. Note villi are not present; there are many lymph nodules in mucosa and submucosa. Not all of the muscularis externa has been drawn. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

which is lined by a simple columnar epithelium. Crypts of Lieberkühn are present in the mucous membrane. Except that they are not as abundantly supplied with goblet cells, they are similar to those in the colon. Argentaffine cells and cells of Paneth are both found in the crypts. The tunica propria, between the crypts, is filled with lymph nodules surrounded by a mass of diffuse lymphoid tissue. These nodules possess well developed germinal centers. They penetrate the muscularis mucosae so that they extend from the mucous membrane into the submucosa.

The muscular coat presents the same arrangement of an inner circular and an outer longitudinal layer of smooth muscle fibers as in the small intestine. Some of the fibers of the longitudinal layer may extend into the mesoappendix and completely invest the blood vessels.

The serous coat is formed by the continuation of the mesoappendix around the wall of the appendix.

As age advances degenerative changes take place in the mucosa, which breaks down into a mass of disorganized material with which, in time, the lumen is filled. As the degeneration of the mucosa progresses, the epithelium is destroyed, only portions of the crypts and a few of the fibers of the muscularis mucosae remaining.

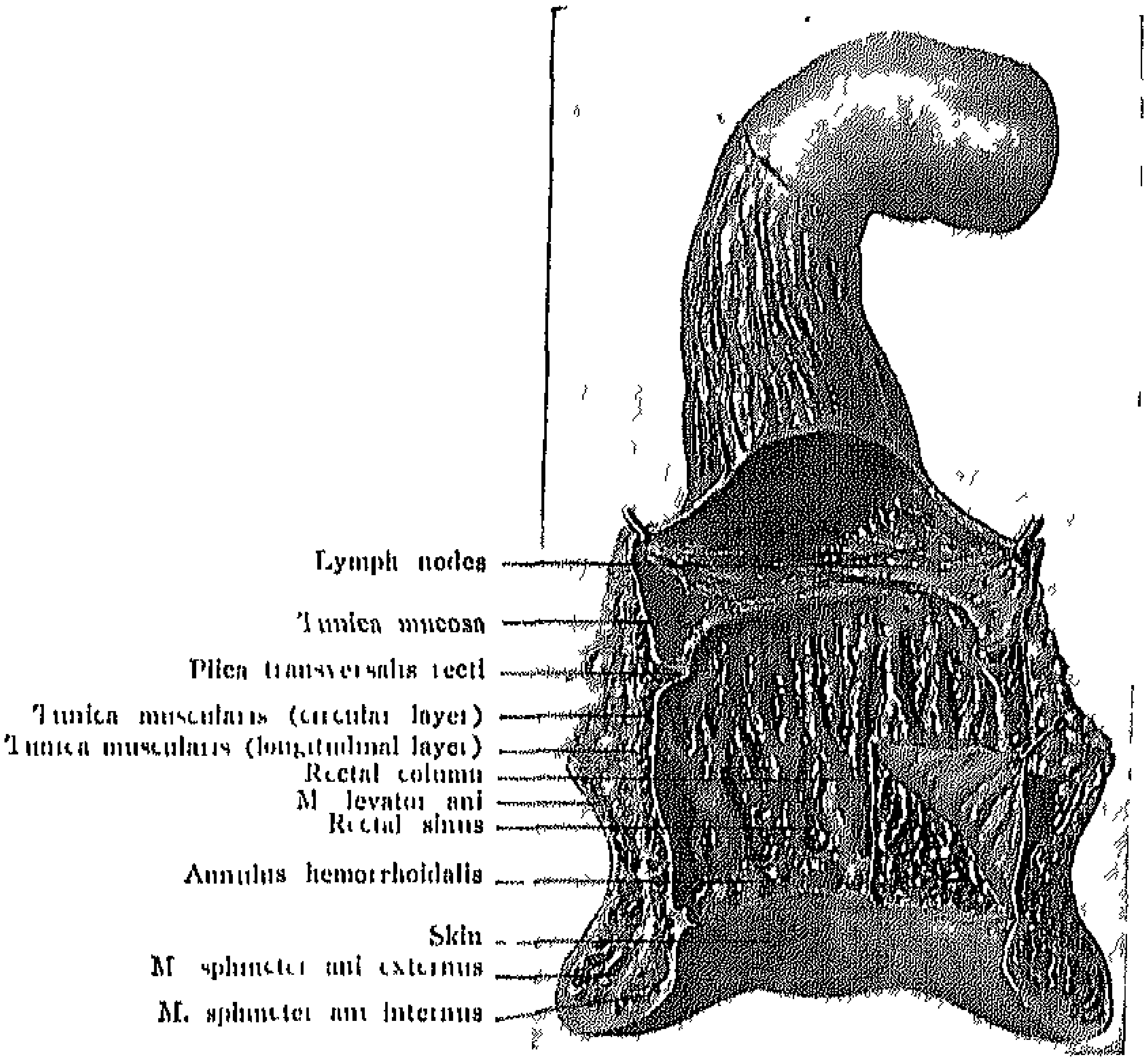

Lymph nodes
Tunica mucosa
Plica transversalis recti
Tunica muscularis (circular layer)
Tunica muscularis (longitudinal layer)
Rectal column
M. levator ani
Rectal sinus
Annulus hemorrhoidalis
Skin
M. sphincter ani externus
M. sphincter ani internus

Fig. 111. Rectum, opened and seen from the front.

THE RECTUM

The sigmoid colon ends in the expanded portion of the alimentary canal which lies between it and the anal canal. This short, expanded portion is known as the *rectum*.

Some authors regard the rectum and the anal canal as parts of the same structure; the anal canal being the lower portion of the rectum (*pars analis recti*).

The wall of the rectum is somewhat thicker than that of the colon, although its coats or tunics are the same as those which have been described for other parts of the alimentary tract.

The mucous membrane contains numerous tubular crypts, which differ from those in the colon by being somewhat longer and wider, and in containing a greater number of goblet cells. A number of solitary lymph nodules may be present in the mucosa.

The inner circular layer of the external muscular coat is continued from the colon without any perceptible change. The longitudinal fibers of the taeniae combine to form a single layer which may be considerably thickened on one, or on two, of the sides of the rectum.

The serous membrane which invests the sigmoid colon extends only a short distance on the wall of the rectum, the greater part of which is enveloped by an adventitia of loosely arranged connective tissue fibers.

A series of transverse folds, the *valves of Houston*, project into the tube and extend from a third to three-fourths of the way around its wall. These folds not only include the mucosa and submucosa, but also portions of the muscular layers.

THE ANAL CANAL

As the wall of the rectum passes into that of the anal canal, it is thrown into a series of longitudinal folds, the *anal columns*, or *columns of Morgagni*. The lower ends of the columns are united to form ringlike folds, which pass transversely around the wall of the canal, the *anal valves*. The grooves between the columns *(anal sulci)* extend downward and end behind the valves in a number of blind pouches, the *anal sinuses*.

As the simple columnar epithelium of the rectum passes into the anal canal, it becomes a two or three layered stratified columnar epithelium, which may be invaginated to form a few cryptlike glands. The lower portions of the columns are covered by a stratified squamous epithelium, which extends over the ridges from below. The stratified columnar epithelium is continued in the grooves (sulci) between the columns. At about the level of the anal valves the canal is lined by a thick, papillated layer of stratified squamous epithelium. This is continued to the border of the anal opening, where it gives place to the thinner epidermis which covers the cutaneous surface. The layer of stratified epithelium below the anal valves, and the epidermal layer, rest on a corium of closely interwoven connective tissue fibers. Above this the subepithelial connective tissue is in the form of a submucosa. The more loosely arranged connective tissue, external to the corium, contains numerous blood vessels and small Pacinian corpuscles.

The muscularis mucosae of the rectum spreads out as it approaches the anal canal, its fibers passing in the form of small bundles, into the anal column as the *dilator muscle of Rudinger*.

The circular layer of smooth muscle fibers ends in a thickened muscular ring at the level of the anal valves, the *internal sphincter muscle of the anus*. External to, and a little below the internal sphincter, bundles of striated fibers are grouped together to form the *external sphincter muscle*. The fibers of the longitudinal layer of smooth muscle pass between the internal and external sphincter muscles to end in the dense fascial tissue of the corium. A number of striated muscle fibers external to the longitudinal layer, belonging to the levator ani muscle may be seen in sections.

Branched tubular structures, the *intramuscular glands*, are located

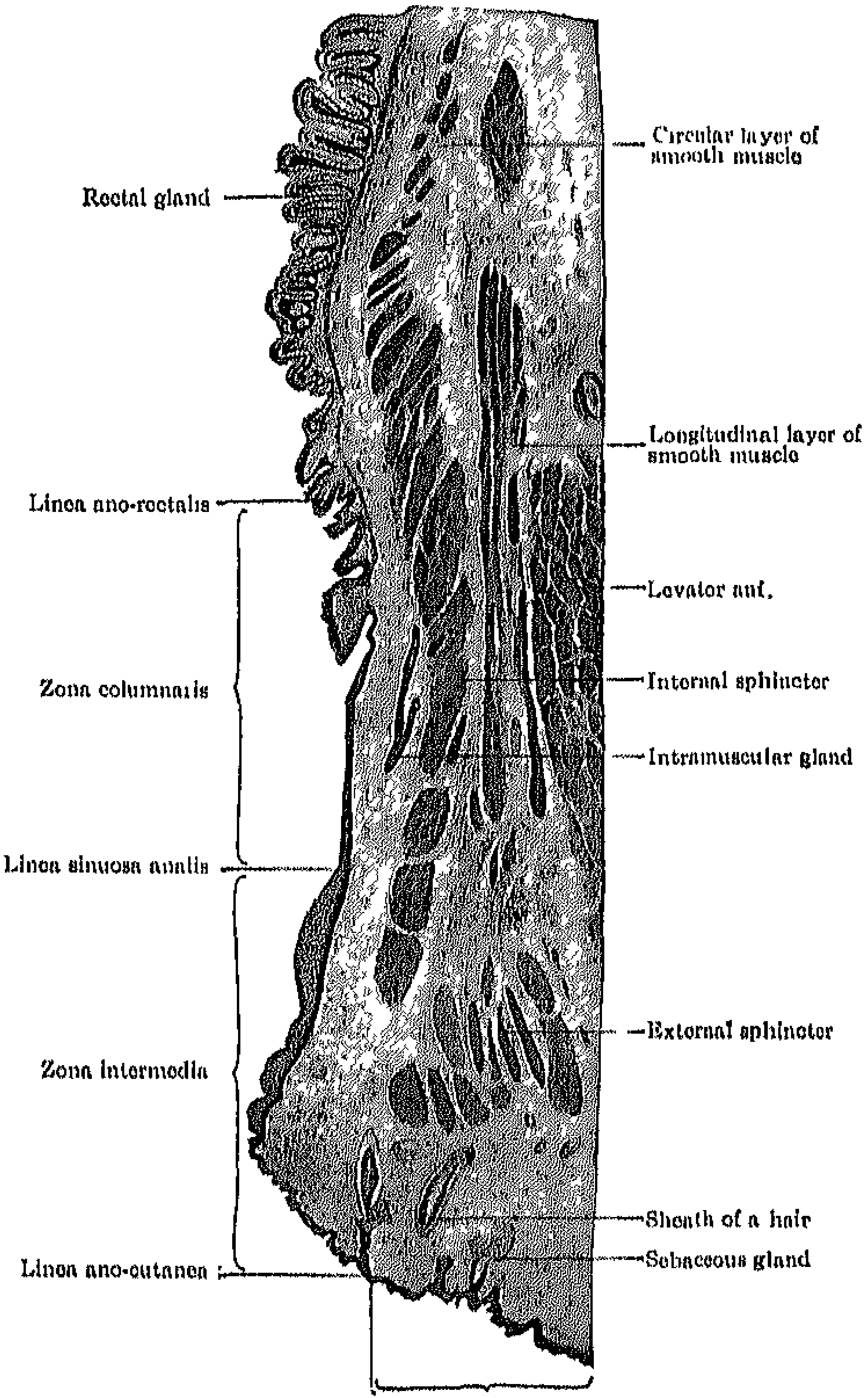


FIG. 145. Longitudinal section through the pars analis recti. From a human embryo of 187 mm. (about four months). (F. P. Johnson) (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

in the connective tissue between the circular and longitudinal layers of the smooth muscle and in the septa between the bundles of the circular layer. These tubules are lined by a one or two layered epithelium of low columnar cells. The tubules unite to form a duct, the epithelial lining of which is several layers of cells in depth and which extends obliquely downward to open on the surface of the epithelium of the canal. The ducts frequently present cystlike enlargements. These glands are relatively few in number.

A few sebaceous glands are located below the level of the internal sphincter muscle and are not associated with hair follicles. A number of large, coiled tubular glands, similar in appearance to sweat glands, are present in the area external to the border of the anal opening.

The following zones have been designated according to the changes which take place in the form of the epithelium in the anal canal. The region occupied by columns of Morgagni is known as the columnar zone *(zona columnaris)*. The upper limit of this zone is indicated by the line that marks the transition from the simple columnar epithelium of the rectum to the stratified columnar epithelium which covers the upper part of the anal columns, the *ano rectal line (linea ano rectalis)*. Below the anal valves, the region which is lined by a layer of stratified squamous epithelium, is known as the *intermediate zone (zona intermedia)*. The epithelium from this zone extends upward on the anal columns for varying distances, the line formed by its meeting with the stratified columnar epithelium being quite irregular, the *linea sinuosa analis*. At the border of the anal opening the epithelium of the intermediate zone merges into the thinner epidermal layer over the cutaneous zone, *zona cutanea*. The line which marks the transition between the intermediate and cutaneous zones being known as the *linea ano cutanea*.

SUMMARY

The digestive system consists of the:

- A. Alimentary tract proper
  - 1. Mouth
  - 2. Pharynx (oral and laryngeal portions)
  - 3. Esophagus
  - 4. Stomach
  - 5. Small intestine
    - a. Duodenum
    - b. Jejunum
    - c. Ileum
  - 6. Large intestine
    - a. Colon
      - (1) Caecum
        - (a) Appendix
      - (2) Ascending colon
      - (3) Transverse colon
      - (4) Descending colon

            - (5) Sigmoid colon
            - (6) Rectum
            - (7) Anus
- B. Accessory structures and glands
    - 1. Teeth
    - 2. Tongue
    - 3. Salivary glands
        - a. Parotid
        - b. Submaxillary
        - c. Sublingual
    - 4. Liver
        - a. Gall bladder
    - 5. Pancreas

The wall of the alimentary tract, from the pharyngoesophageal junction to the rectoanal junction, has a common structural plan which is:

1. Mucosa
    - a. Epithelium
    - b. Tunica propria
2. Muscularis mucosae
3. Submucosa
4. Muscularis externa
5. Serosa—covering almost all of the tract below diaphragm or
   Adventitia—forming external coat of esophagus and part of the rectum below extent of peritoneum

DIGESTIVE TRACT
GENERAL STRUCTURAL CHARACTERISTICS

Region	*Mucosa*		*Muscularis Mucosae*	*Submucosa*
	Epithelium	*Tunica Propria*		
Pharynx (Oral and laryngeal portions)	Stratified squamous	Relatively thick layer	Elastic fibers arranged mostly in a longitudinal direction	No well defined layer on posterior and lateral walls Distinct layer present on anterior wall
Esophagus	Stratified squamous	Moderately thick layer	Relatively thin layer of smooth muscle	Relatively thick layer
Stomach	Simple columnar	Relatively thick layer	Relatively thin layer of smooth muscle	Moderately thick layer
Small Intestine	Simple columnar	Variable thickness	Well developed layer of smooth muscle	Variable thickness
1. Duodenum		Relatively thick layer		Relatively thick layer
2. Jejunum		Relatively thin layer		Relatively thin layer
3. Ileum		Relatively thin layer		Relatively thin layer
Large Intestine	Variable changes at rectoanal junction			
1. Colon	Simple columnar	Thick layer	Well developed layer	Moderately thick
2. Rectum	Simple columnar	Slightly thicker than in colon	Well developed layer	Moderately thick
3. Anus	Stratified columnar to stratified squamous	Absent Corium present	Spreads to form dilator muscle of Rudinger	Thin layer
4. Appendix	Simple columnar	Relatively thick	Poorly defined layer	Moderately thick

NOTE: Tabular material refers to typical area of each segment. Attention should be called to the fact that changes in structure are gradual and the point at which change occurs is somewhat variable, except at gastroesophageal and gastroduodenal junctions, where changes are abrupt.

DIGESTIVE TRACT
GENERAL STRUCTURAL CHARACTERISTICS

Region	*Muscularis Externa*	*External Layer*	*Arrangement of Lymphoid Tissue in Tunica Propria*
Pharynx (Oral and laryngeal portions)	Striated muscle Layers not very definite	Connective tissue	Numerous lymphocytes in form of diffuse aggregations and occasional small nodules
Esophagus	Upper ⅓—striated muscle Middle ⅓ { striated muscle smooth muscle Lower ⅓—smooth muscle	Adventitia	Aggregations of diffuse lymphoid tissue Occasional small nodules
Stomach	Smooth muscle Inner—oblique Middle—circular Outer—longitudinal Inner and middle layers are thickened to form pyloric sphincter	Serosa	Diffuse lymphoid tissue Small nodules in pyloric end of stomach
Small Intestine	Smooth muscle { Inner—circular Outer—longitudinal layer	Serosa	Diffuse lymphoid tissue. Nodules in varying arrangements (solitary and aggregations)
1. Duodenum			Diffuse lymphoid tissue Solitary nodules
2. Jejunum			Diffuse lymphoid tissue Solitary nodules
3. Ileum			Aggregations of lymph nodules known as Peyer's patches. Diffuse lymphoid tissue
Large Intestine	Outer longitudinal muscle layer is gathered into 2 or 3 thickened bands	Variable	Diffuse lymphoid tissue and some nodules Nodules may enter submucosa
1. Colon	3 thickened bands called taenia coli	Serosa—Partial covering	Few solitary nodules which may extend into submucosa
2. Rectum	2 thickened bands	Serosa in upper part Adventitia in lower part	A number of solitary nodules and some diffuse lymph tissue
3. Anus	Inner circular ends as internal sphincter External layer terminates in fascia External sphincter—striated muscle	Adventitia	Few scattered lymphocytes
4. Appendix	Smooth muscle	Serosa	Filled with lymph nodules Extend into the submucosa

Variations in Mucosal Layer of the Digestive Tract from the Pharyngoesophageal Junction to the Rectoanal Junction

Region	*Epithelium*	*Villi*	*Gastric Pits*	*Simple Tubular Glands Only*	*Plicae Circulares*
Esophagus	Stratified squamous	Absent	Absent	Absent	Absent
Stomach	Simple columnar	Absent	Present	Absent	Absent
1. Fundus			Short and wide		
2. Pylorus			Long and narrow		
Small Intestine	Simple columnar	Present	Absent	Absent	Present
1. Duodenum		Broad, tall and leaf-like			Low and broad First appear near middle portion
2. Jejunum		Tall and conical			Tall, thin and branched
3. Ileum		Shorter than in jejunum and club-shaped			Much lower and somewhat wider than in jejunum
Large Intestine	Simple columnar	Absent	Absent	Present	Absent
1. Colon				Somewhat shorter and narrower than those in rectum	
2. Rectum				Somewhat longer and wider than those in the colon	

Variations in Mucosal Layer of the Digestive Tract from the Pharyngoesophageal Junction to the Rectoanal Junction

Region	Taenia Coli	Glands		
		Name and Type	*Location*	*Secretion*
Esophagus	Absent	1 Esophageal or deep glands Branched tubular 2 Cardiac or superficial Branched tubular	Submucosa Tunica propria	Mucous Mucous and serous
Stomach	Absent	Present		
1. Fundus		1 Gastric glands Simple tubular	Tunica propria	Mucous HCl Pepsin
2. Pylorus		1. Pyloric glands Branched tubular	Tunica propria	Mucous Scant amount of HCl Pepsin
Small Intestine	Absent	Present		Mucous Enzymes Hormones
1. Duodenum		1. Brunner's glands Branched tubular 2. Crypts of Lieberkühn Simple tubular	Submucosa Tunica propria	
2. Jejunum		1 Crypts of Lieberkühn Simple tubular	Tunica propria	
3. Ileum		1 Crypts of Lieberkühn	Tunica propria	
Large Intestine	Present	Present		Mucous
1. Colon	3 thickenings of the longitudinal muscle layer	1 Crypts of Lieberkühn Simple tubular		
2. Rectum	2 thickenings of the longitudinal muscle layer	1. Crypts of Lieberkühn Simple tubular		

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Glands

Epithelium serves not only as a protective layer, but in some areas its cells become modified to produce specific substances or *secretions.* Such cells are known as *gland cells.* These secretions may be required locally (mucus in the intestinal tract) or the secretion may be used at a point some distance from the secreting cells (bile, produced by the hepatic cells and used in the small intestine), or the substances produced by the cells may be added to the waste material of the body (urine).

Glands may be classified in a variety of ways: According to whether their secretory products are secreted directly into the blood or lymph stream *(ductless* or *endocrine glands)* or are carried by means of a more or less complex duct system to be emptied at a point some distance from the secreting cells *(duct* or *exocrine glands).* A few glands have both exocrine and endocrine portions in the same gland (pancreas).

The exocrine glands are further subdivided according to their structure:

A. Unicellular glands (goblet cells)
B. Simple
  1. Tubular
    a. straight
    b. coiled
    c. branched
  2. Branched alveolar or acinar glands
  3. Saccular
C. Compound
  1. Tubular
  2. Alveolar or acinar glands

Glands are sometimes classified according to the kinds of secretion they produce, i.e., *mucous, serous,* or *mixed glands;* or they may be classified according to the way in which they expel their secretions, as merocrine, apocrine, or holocrine glands.

ENDOCRINE GLANDS

These glands consist of cords or masses of closely arranged epithelial cells having a stroma of very delicate connective tissue, or of saclike structures (follicles) lined by epithelium and held together by a more dense connective tissue stroma. One characteristic of all endocrine glands is their extreme vascularity. Blood and lymph vessels lie in close relation with the epithelial cells which secrete their materials directly into the blood and lymph systems to be carried throughout the entire body. These glands have no duct system of any kind. The endocrine glands are: the *thyroid*, *parathyroids*, *adrenals*, *hypophysis*, *islands of Langerhans* in the pancreas, the *interstitial cells* of the testes, and the *corpus luteum* of the ovary.

EXOCRINE GLANDS

The simplest form of secreting structure is a single cell *(unicellular gland)* which in man is represented by *goblet cells*. These cells occur throughout the epithelial layer lining parts of the respiratory tract and throughout the alimentary tract. In the alimentary tract, for example, some of the cells scattered throughout the epithelium lining the tract, modify and produce a substance, *mucus*. This material is a thick, slippery secretion which is expelled from the cell onto the surface of the epithelium where it forms a protective coating for the entire epithelial layer, and in the lower part of the tract it serves as a lubricating substance as well.

The mucus of the goblet cell is produced in the cytoplasm of the cell, where it first appears in the form of small granules in the apical portion of the cell and in relation to the Golgi apparatus. These small granules coalesce and eventually the large globule of dense mucus entirely fills the apical portion of the cell. It pushes the nucleus and the cytoplasmic substance toward the base of the cell where they are compressed. When the cell is ready to discharge its secretion, the membrane on the free end of the cell may rupture and the mucus may be extruded into the lumen of the intestine. At other times the mucus may escape more gradually, as it is formed. In the first instance the cell collapses and undergoes a period of rest and regeneration after which the secretory phase is again repeated. Thus gland cells undergo periods of rest and secretion and it is possible to find cells in various stages of activity.

It is not known just what structures of the cell are primarily responsible for the formation of secretions. Undoubtedly both the Golgi apparatus and the mitochondria play some part in the formation of secretion, but just how it is brought about is unknown.

Except for the goblet cell, all other types of glands are multicellular.

In all multicellular glands there is a structural and functional differentiation of the cells. First there is an increase in the cells with a subsequent invagination, either confined to the epithelial layer or as more commonly occurs, extending into the underlying connective tissue (tunica propria or the stroma). In certain regions the secreting elements may extend into the submucosa (Brunner's glands of the duodenum). This is followed by a functional differentiation of the invaginated cells. Some of the cells, usually those in the deepest part of the invaginated cell group (fundus), take over the secreting function. The cells connecting these secreting cells with the surface epithelium act to transport the secretory products to the surface. These cells form the excretory duct system. By repeated division and growth the complexity of the gland develops. In a few instances some of the cells lining the duct system nearest the secreting structures may also assume a limited secretory function (salivary glands).

There are three types of secretory terminal end pieces in glands. The terminal secretory portion of the gland may appear simply as the fundic area of a tubelike invagination of the epithelial layer, or the secreting areas may consist of tall pyramidal cells arranged about a lumen. These secreting structures may be elongated and sausage-shaped, the so-called *alveolar end pieces,* or they may form round ball-shaped structures known as *acinar end pieces.* The cells lining the ducts nearest these secreting end pieces are usually low cuboidal or cuboidal in shape and stand out sharply from the secreting portion of the gland. On these secreting cells there are usually terminal bars along their free surfaces and in many of these glandular end pieces, small canals extend from the lumen and penetrate between the cells. These canals end blindly and may branch. The walls of these canals are formed by the cell membrane. The canals serve to increase the surface for the elimination of the secretion. A further modification is seen in the parietal cells of the stomach, which show a system of extremely fine intracellular canals which serve a similar purpose.

Multicellular glands may be divided structurally into: *simple* and *compound* glands. Simple glands may have only a secreting portion which opens on an epithelial lined surface or it may have a duct. Such a duct will be unbranched and the secretory portion which empties into it may show a variety of forms: simple, branched, or coiled tubular structures, or alveolar or acinar end pieces.

Compound glands, on the other hand, are more complex in structure. However, they consist essentially of many simple glandular elements joined together by means of a system of ducts which ultimately drains the secretion from all of the "simple glands" and empties eventually on an epithelial lined surface. Their end pieces are most often alveolar or acinar in shape.

UNICELLULAR GLANDS (Goblet Cells)

SIMPLE GLANDS

TUBULAR. a. SIMPLE STRAIGHT TUBULAR GLANDS. They consist of short, straight, epithelial lined, invaginated tubules. The lumen is the same diameter throughout and it has no excretory duct, but opens directly onto the surface of the epithelium. (Ex.: crypts of Lieberkühn of the intestine.)

b. SIMPLE COILED TUBULAR GLANDS. They have a relatively long excretory duct and a long secretory portion which coils on itself to form a knotlike end portion. (Ex.: sweat glands.)

c. SIMPLE BRANCHED TUBULAR GLANDS. These glands may or may not have an excretory duct. The secretory portion is tubular and may show a variable number of branches. The terminal portions may be very slightly coiled or bent. (Ex.: branched tubular, no duct: pyloric glands of the stomach; branched tubular with excretory duct: Brunner's glands of the duodenum.)

BRANCHED ALVEOLAR OR ACINAR GLANDS. In this type of gland a number of alveolae or acini empty along a single duct. Usually the end piece is of the acinar type. (Ex.: Meibomian glands of the eyelid.)

SACCULAR. These glands present no true lumen. They consist of a compact group of secreting cells arranged in a saclike mass. The size and, therefore, the number of secreting cells is variable. These cells expel their secretion by themselves disintegrating as they approach the neck or mouth of the gland. (Ex.: sebaceous glands.)

COMPOUND GLANDS

COMPOUND TUBULAR GLANDS. The excretory duct consists of a number of branching tubules lined by a simple (or pseudostratified) epithelium. The secretory portion is also tubular; they usually branch and their terminal portions coil slightly. (Ex.: cardiac glands of the stomach and the pure mucous glands of the mouth.)

COMPOUND ALVEOLAR OR ACINAR GLANDS. These glands are more

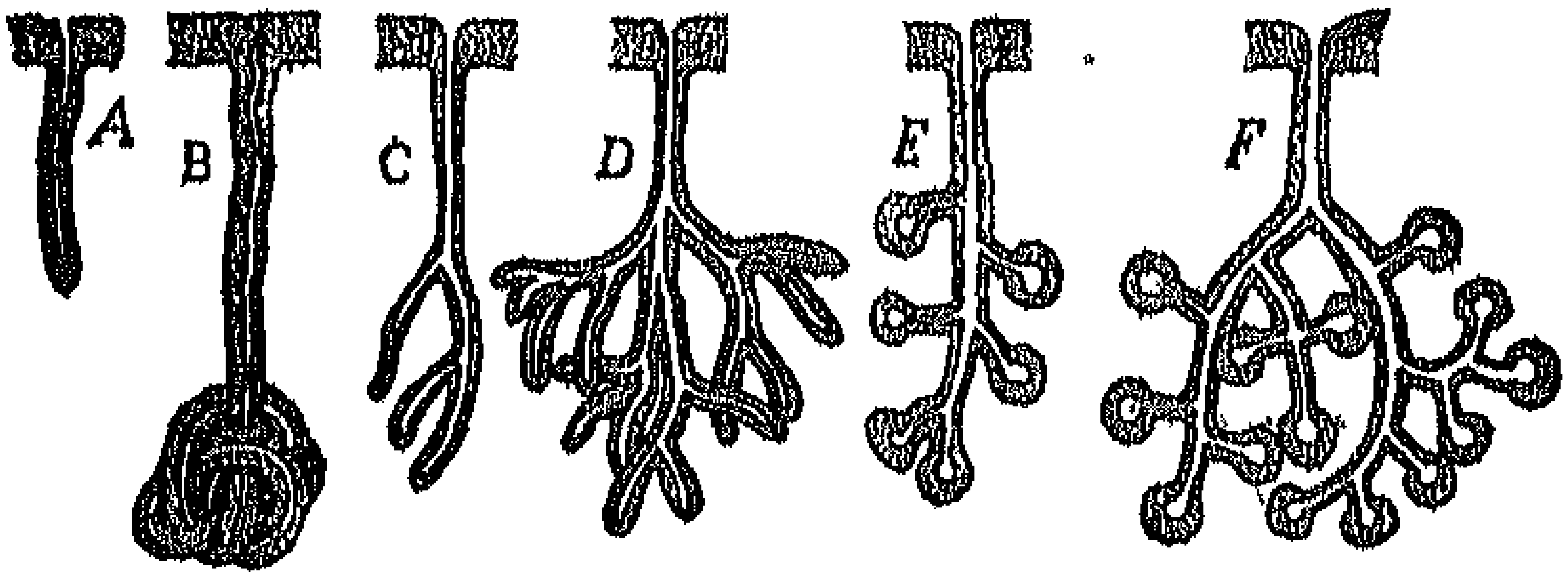

FIG. 146. Diagrams of simple exocrine glands. (A) Simple tubular. (B) Simple coiled tubular. (C and D) Simple branched tubular. (E and F) Simple branched acinous. (Courtesy, Kingsley: "Comparative Anatomy of Vertebrates," Philadelphia, The Blakiston Company.)

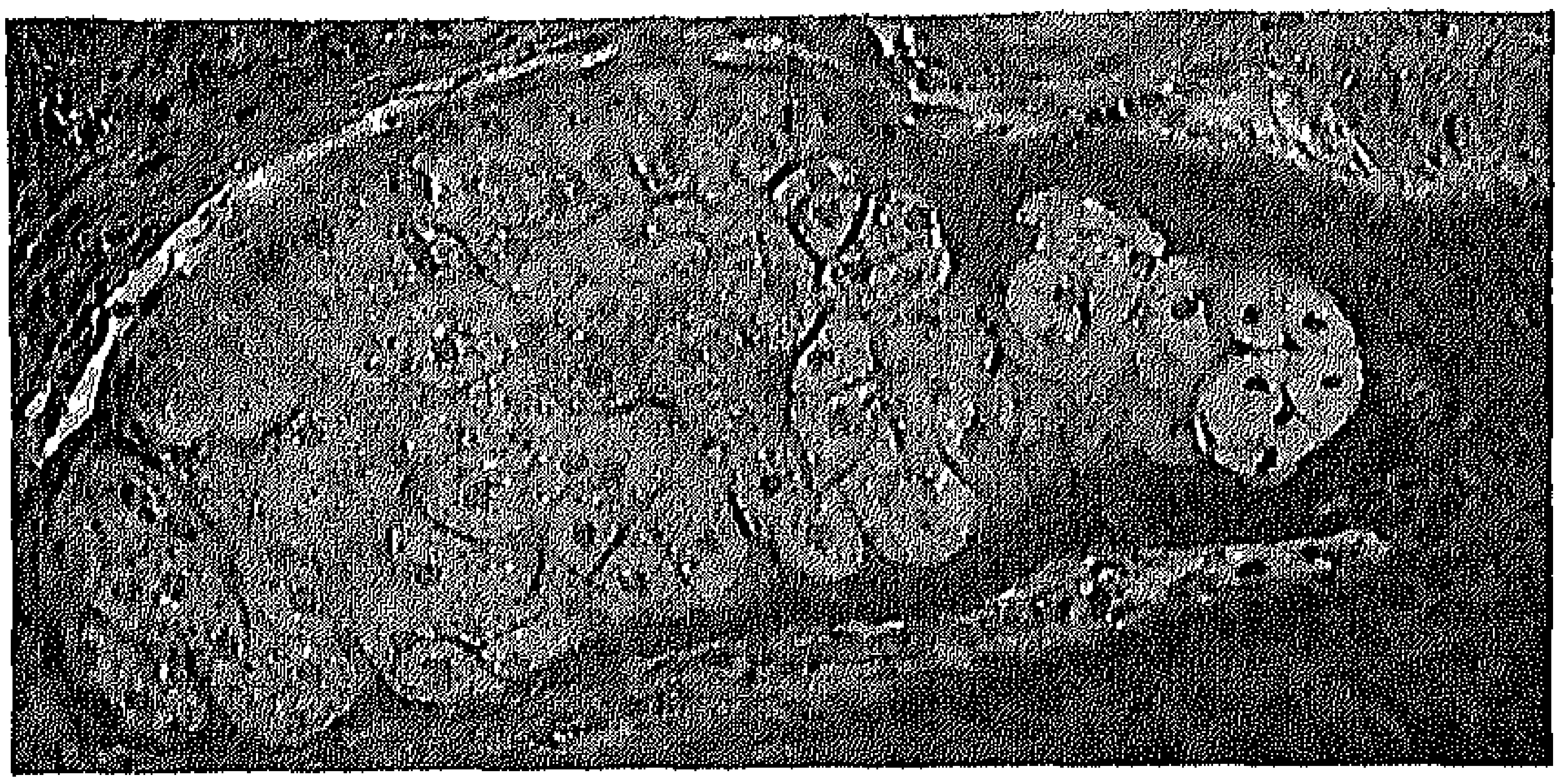

FIG. 147. *Saccular gland (human sebaceous gland). This type of gland is a solid mass of cells. It contains no lumen and no true duct system. Photomicrograph.*

properly called tubuloalveolar or tubuloacinar glands since many of their secreting elements are tubular. The duct system is complex and is lined by a variety of epithelial cells arranged from a simple to a stratified layer. Sometimes all of the ducts empty into a single large duct; in other cases several ducts may represent the terminal portion of the duct system. If there are a number of round secreting end pieces among the tubular structures, the gland is referred to as tubuloacinar; if they are alveolar in shape it is a tubuloalveolar gland. The compound glands are: the salivary glands, the pancreas (except the islands of Langerhans), etc.

Glands are often referred to as mucous, serous, or mixed glands depending on the kind of secretion which they produce. The acini in each case is very typical and microscopic examination will identify them. The acini of both mucus and serous secreting glands consist of pyramidal cells arranged around a central lumen. The mucous acini are characterized by the clear cytoplasmic area which contains, or did contain, the mucous secretion. The nuclei are dark staining and flattened against the base of the cell. The lumina of mucous acini are larger than those of serous acini in order to allow for the exit of the thicker mucoid secretion. The mucus is usually colorless and appears as a clear space. Serous acini, on the other hand, are made up of cells that have a granular cytoplasm, the size and number of granules depending on the secretory activity of the cell. The nuclei are round and more lightly staining and usually centrally placed. They are never flattened against the basal portion of the cell. Some mucous acini may be "capped" by one or more serous cells. These cells (demilunes) fit over the basal edge of the mucous cells and are semilunar in shape. Their cytoplasm is granular and their nuclei round and in the center of the cell. Their secretion reaches the lumina of the mucous acini either by a narrow protrusion of the cell which extends between the mucous cells or by way of intercellular secretory canaliculi. It is thought that the serous secretion thins the heavy mucoid material produced by the mucous acini.

Glands are sometimes classed as merocrine, apocrine, or holocrine glands, depending on their method of expelling their secretion. In merocrine glands the secretion is expelled without damage to the cell. It secretes, rests and secretes again. Most of the glands of the body secrete in this manner. In apocrine glands the entire apical portion of the cell is expelled with the secretion. From the nucleus and cytoplasm remaining in the basal portion of the cell, the cell is able to regenerate and secrete again (ex.: mammary gland). Holocrine glands show destruction of the entire cell which degenerates by fragmentation. The fragmented cell and its secretion represents the secretory material. New cells are produced to replace those destroyed by the activity of the gland (ex.: sebaceous gland).

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Glands Associated with the Digestive Tract

Besides the glands that are in the submucosa and mucosa of the digestive tube proper, there are several large compound glands which are accessory organs of the digestive system. These glands lie outside the digestive tract but are connected to it by way of their terminal ducts, and the secretions which they produce are emptied into the digestive tube. These secretions are important for the proper digestion and assimilation of the various food elements. The glands are: the *salivary glands,* the *pancreas,* and the *liver* with its attached gall bladder.

THE SALIVARY GLANDS

The salivary glands are large *tubuloacinar (tubuloalveolar)* structures which are associated with the oral cavity and produce a secretion known as *saliva.* The principal salivary glands are: the *parotid,* the *submaxillary* and the *sublingual glands.* Besides the secretions produced by these glands, the saliva receives additional secretions from the labial, buccal and lingual glands which are located in the mucous membrane of the oral cavity.

The Parotid Gland

The parotid gland is located just beneath the skin and occupies a depressed area or fossa between the ear and the ramus of the mandible. It is enclosed by a dense fibrous capsule (upward extension of the deep fascia of the neck) from which connective tissue septa pass into its substance. The connective tissue septa form the stroma by which the parenchyma of the gland is supported. These connective tissue septa also furnish support for the system of ducts, blood vessels and nerves which extend into the gland.

In man, the parenchyma is made up almost exclusively of serous acini whose secretion reaches the oral cavity by way of a complex duct system.

The secreting portions of the gland consist of acinar or alveolar type end pieces. The cells are pyramidal in shape and are grouped about a lumen which, in the resting cell, is so small that it is practically obliterated. During periods of secretory activity the cells diminish in size and the lumen becomes somewhat larger. Basal cells have been reported to be present.

The secreting cells have a lightly basophilic staining cytoplasm. In the resting stage it is filled with fine presecretory or zymogen granules which are most distinct between the nuclei and the free surfaces of the cells. After a period of prolonged activity the granules disappear, but are formed again following a period of rest. Basal striations are present and are especially evident after periods of prolonged activity. The striated appearance is due to the presence of small rodlike structures which are supposed to be related to the production of presecretory granules. The nuclei are round and centrally located. They stain sharply with hematoxylin.

Beginning at the acini, the named portions of the duct system are: *intercalary (intermediate) ducts, intralobular (salivary) ducts, inter-*

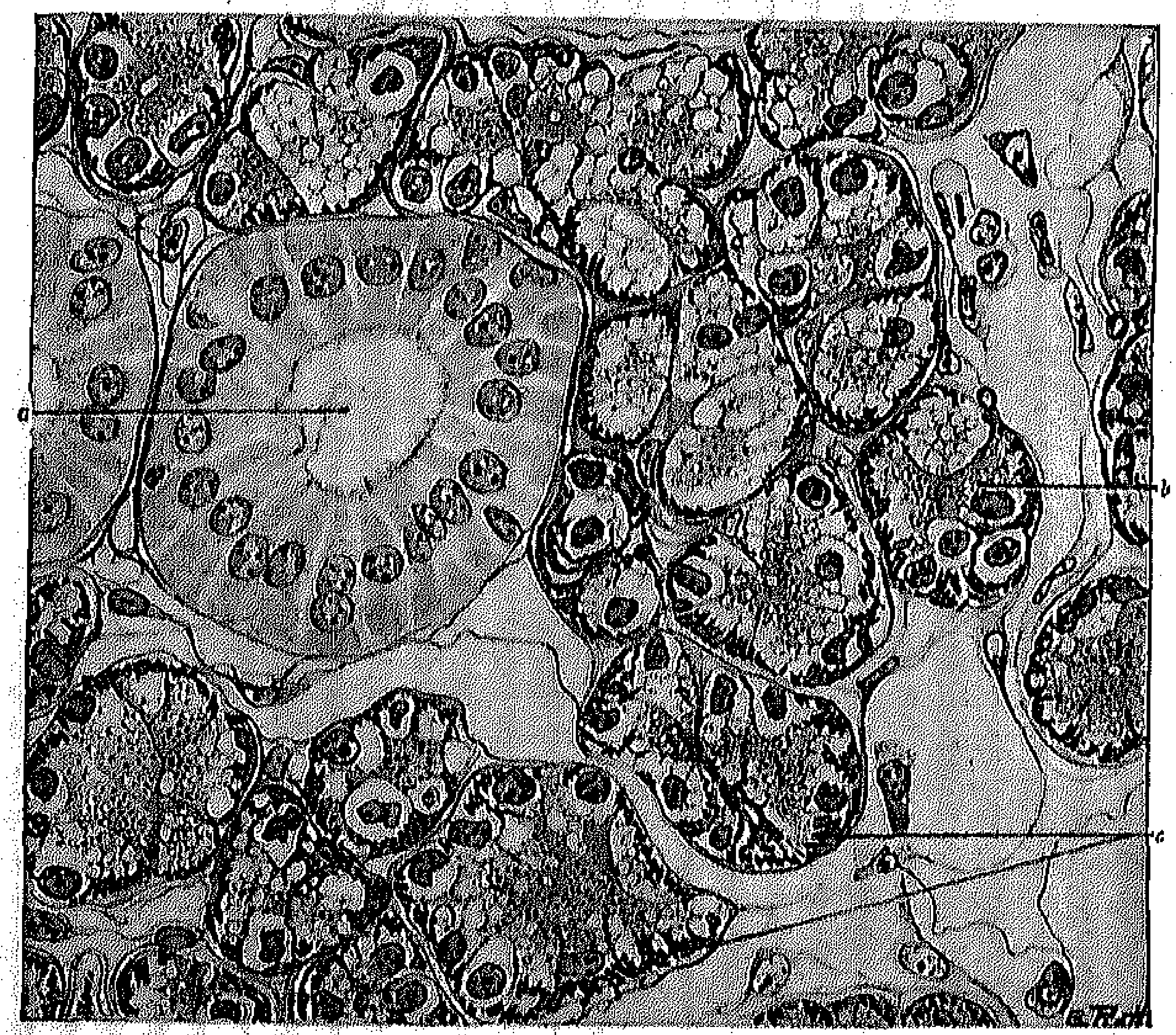


FIG. 148. Section of a human parotid gland. Zenker fixation; methylene blue and eosin. *(a)* Section of a duct. *(b)* Secretory cell. *(c)* Basal striations. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

lobular ducts, interlobar ducts and the *main secretory duct (Stensen's duct).*

The intercalary ducts (intermediate) are relatively long. Their epithelium consists of low, flattened cells which are continuous with the cells that form the walls of the acini.

The intralobular (salivary) ducts are lined by a low columnar or cuboidal epithelium. The nucleus is round and centrally placed. The cytoplasm contains fine granules and the basal part of the cells shows striations. These cells have a secretory function and are thought to add water and certain salts to the product of the acinar cells.

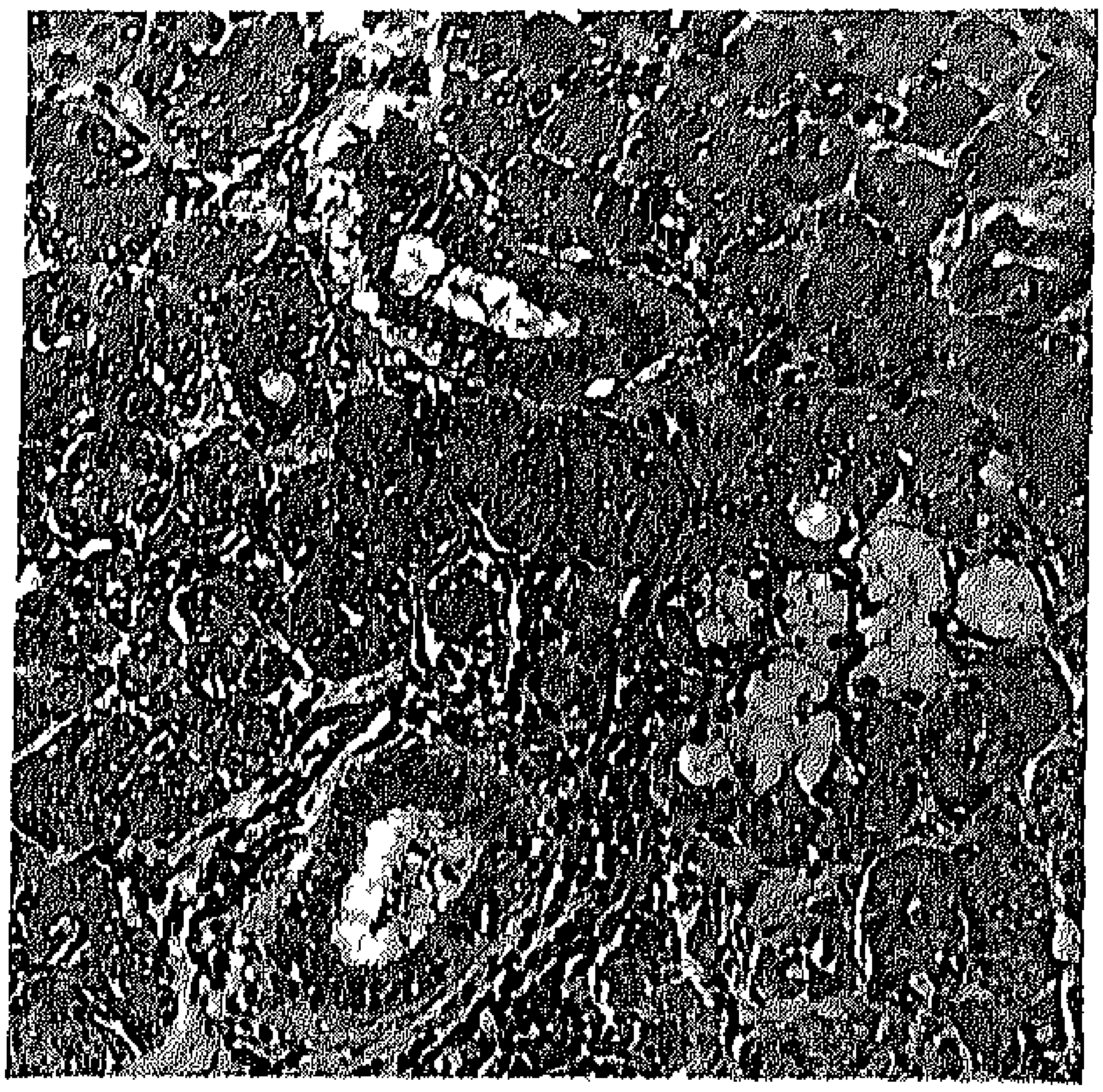


FIG. 149. Section of a submaxillary gland showing serous and mucous acini. Hematoxylin and eosin. Photomicrograph.

The interlobular ducts are found in the connective tissue septa between the lobules. The first portion of these ducts is likewise lined by a simple columnar epithelium which changes to a pseudostratified columnar in the interlobar ducts. In the interlobular and intralobular ducts, small stellate cells are located between the epithelium and the basement membrane. These cells, which are not regularly disposed but occur at irregular intervals, are known as *basket cells.* They can be recognized in ordinary sections by their small, round, deeply staining nuclei. The basket cells send delicate protoplasmic processes about the cells of the epithelium. These processes are believed to contract and thus aid in the passage of the secretion through the ducts.

Stensen's duct passes forward in the tissue of the cheek and opens

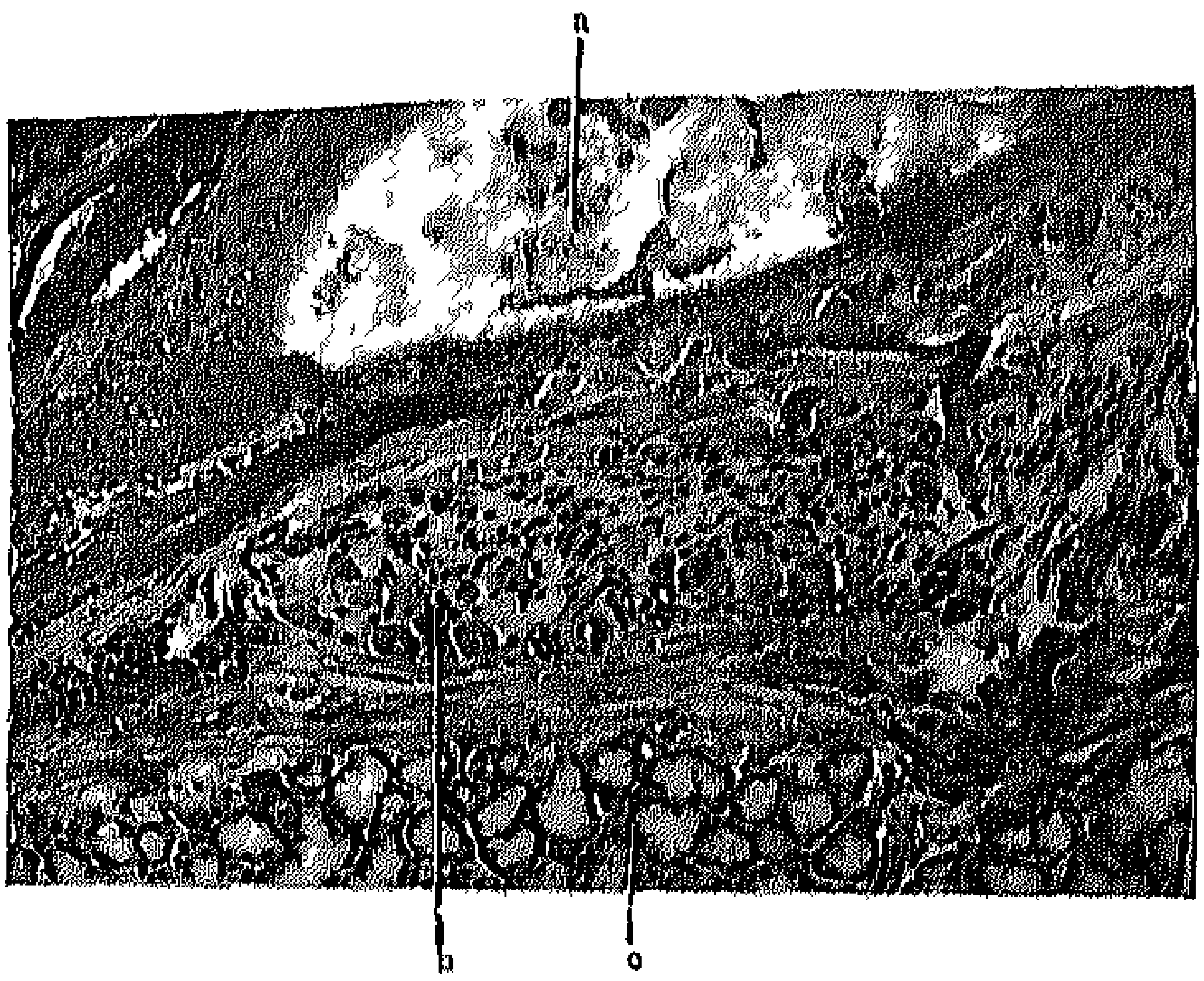


FIG. 150. Section of submaxillary gland, showing a large nerve ganglion in the interlobar connective tissue. (a) Blood vessel. (b) Groups of ganglion cells. (c) Mucus-secreting acini. Photomicrograph.

into the oral cavity opposite the second molar of the upper jaw. The stratified squamous epithelium of the oral cavity is continued into the duct a short distance from its opening, it then becomes a stratified columnar epithelium or pseudostratified columnar epithelium.

The epithelium of the ducts rests on a layer of densely interwoven fibrous tissue.

THE SUBMAXILLARY GLAND

The submaxillary is a mixed gland containing both serous and mucous acini. The proportion of serous to mucous acini varies markedly in different animals. In the dog the gland is predominately mucous, while in man the serous acini are by far the most numerous, constituting about four-fifths of the total number of acini, while the mucous acini make up the other one-fifth.

The gland is enveloped by a capsule of dense fibrous tissue from which septa extend into its substance, dividing it into lobes and lobules. The duct system is essentially the same as that of the parotid gland.

The cells of the serous acini are similar to those of the parotid gland. The cells of the mucous acini are pyramidal in form. The greater part of the mucous cells are filled with a mucoid substance which gives them a clear, homogeneous appearance. The nuclei and a small portion of the cytoplasm are pressed into the base of the cell. They are arranged about a relatively wide lumen. Some of the mucous acini are capped by large, concentric cells called *demilunes* (Heidenhain), or *crescents* (Gianuzzi), which are located between the mucous secreting cells and the basement membrane. These cells have the same structural characteristics as cells of the serous acini. The cytoplasm is filled with numerous presecretory granules and there is a large, round, centrally located nucleus. These cells produce a serous fluid which is chemically similar to that produced by the cells of the parotid gland. Besides the enzyme which they add to the salivary secretions, the watery fluid produced by the demilunes has the effect of thinning the secretion of the mucous cells, thus facilitating its passage through the ducts.

The intercalary (intermediate) ducts which communicate with the serous acini are relatively long, while those which communicate with the mucous acini are short and wide. Owing to the difference in the length of the intermediate ducts to the two types of acini, the intralobular ducts receiving the mucous secretion are considerably longer than those which receive the serous secretion. The cells that line these ducts are similar to those in the parotid gland.

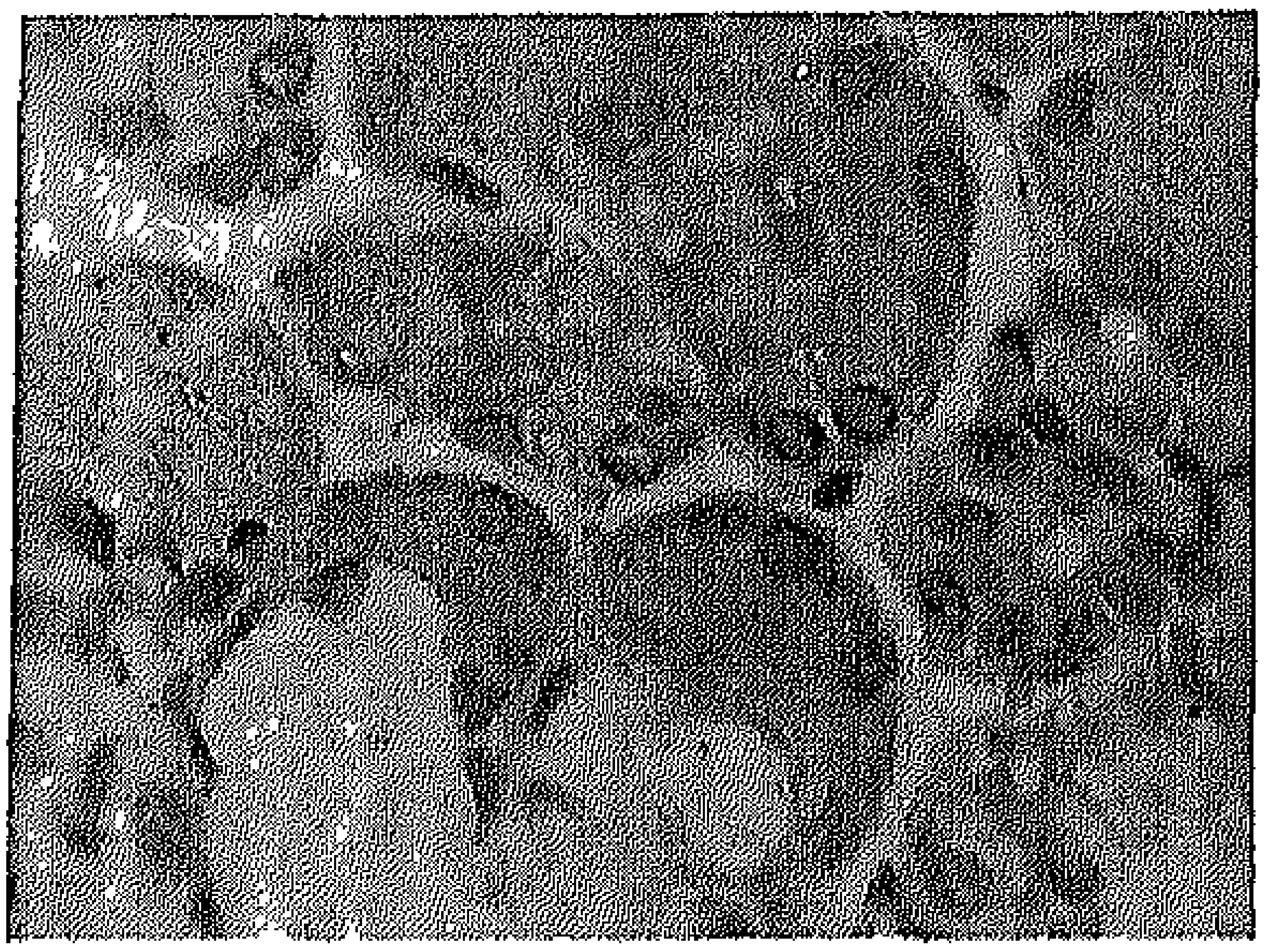


FIG. 151. Portion of submaxillary gland showing mucous acini with "capping" serous demilunes. Photomicrograph.

The intralobular ducts belong to the secretory system as shown by their striations. They are lined by a low columnar or cuboidal epithelium.

The ducts of the excretory portion of the system are the interlobular, interlobar and the main duct (Wharton's).

The interlobular ducts are lined by a simple columnar epithelium which changes into a pseudostratified layer as it continues toward the interlobar duct.

The interlobar ducts are likewise lined by a pseudostratified columnar epithelium.

The principal duct (Wharton's duct) passes forward in the floor of the mouth to open into the oral cavity below the tip of the tongue. The structure of Wharton's duct is similar to that of Stensen's duct, except that its walls are somewhat thicker and contain a greater amount of smooth muscle tissue.

THE SUBLINGUAL GLANDS

The sublingual glands consist of small groups of glandular structures located below the tip of the tongue in the connective tissue which forms the floor of the oral cavity. Each gland communicates with the oral cavity by its own duct, the openings of the ducts being located in small, papillalike elevations, which form a row on either side of the frenulum. Although the sublingual glands are mixed mucous and serous structures, the mucous acini greatly predominate. Demilunes are also present. A distinct connective tissue capsule around the glands is lacking.

The duct system is quite simple compared with that of the other salivary glands. There are no intermediate ducts, the acini being connected directly with the intralobular ducts.

BLOOD AND NERVE SUPPLY OF THE SALIVARY GLANDS. The blood vessels which supply the salivary glands enter through the

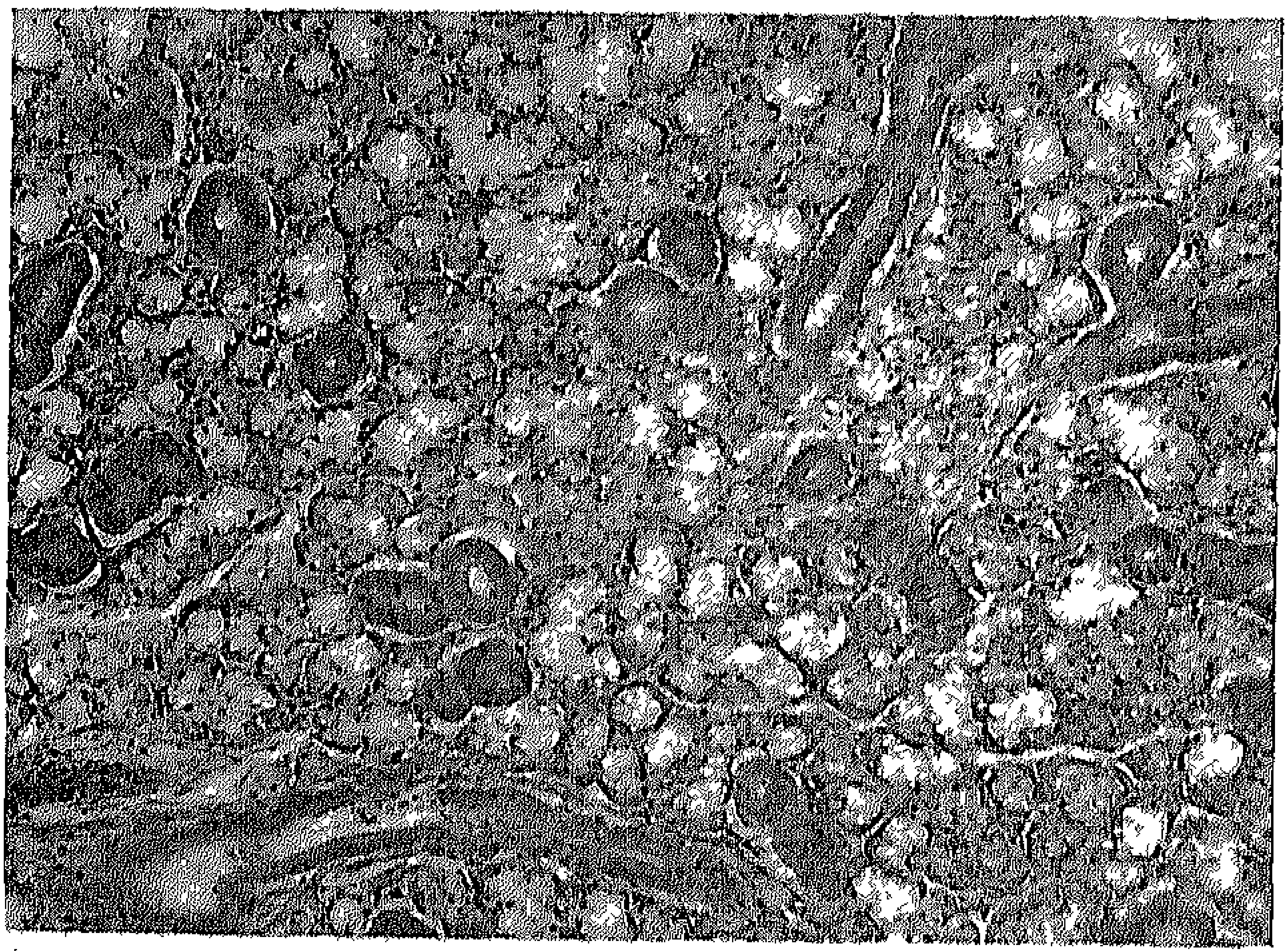


FIG. 152. Section from a sublingual gland showing ducts, mucous and serous acini. Photomicrograph.

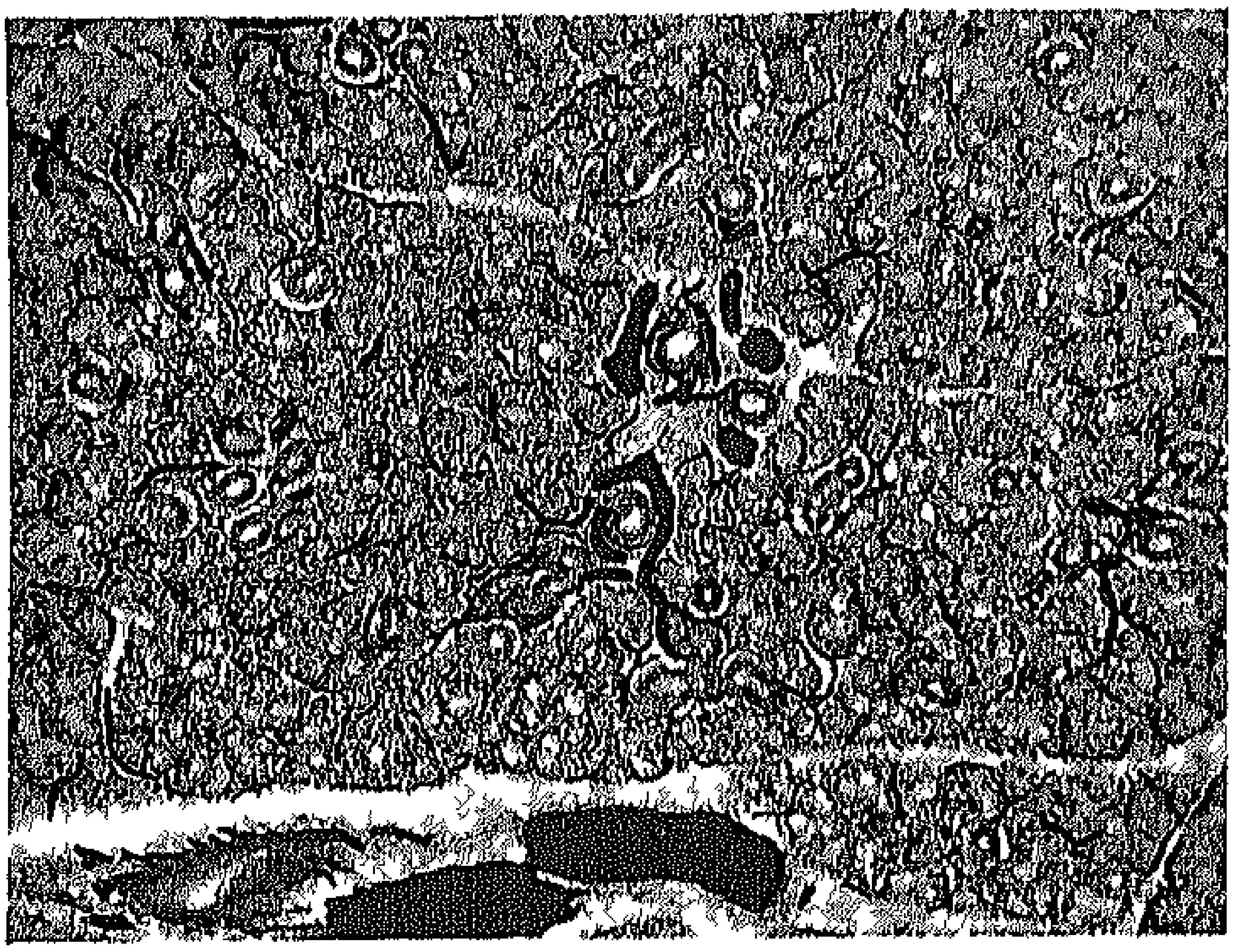


FIG. 153 Injected salivary gland showing the interlobular vessels and their relations to the interlobular ducts their intralobular branches and the capillaries winding about the acini The spaces and lines in black are the blood vessels and their capillary branches Photomicrograph

capsule and their branches follow the distribution of the ducts, which they accompany in the connective tissue septa. According to their position in relation to the lobes and lobules they are known as interlobar, interlobular, and intralobular vessels. The intralobular vessels break up into capillaries which wind around the walls of of the acini. The veins are in the same relation to the lobes and lobules as the arteries, which they follow in their course from the glands.

The lymphatics, which are not abundant, originate in capillary networks about the acini. The capillaries unite to form the larger vessels which are located in the connective tissue septa. These vessels leave the glands to drain into the cervical lymph nodes.

The salivary glands are supplied by both myelinated and unmyelinated nerve fibers. The myelinated fibers lose their sheaths and end in the walls of the ducts. The unmyelinated fibers are from the autonomic system and supply the walls of the blood vessels, and they also extend among the cells of the acini. Some of the fibers end in relation to groups of ganglion cells which are located in the septa in association with the larger blood vessels.

THE PANCREAS

The pancreas is one of the accessory organs of the digestive system. It consists of two distinct types of glandular elements: *exocrine* and *endocrine* glands. The elements of the exocrine portion elaborate secretions that are emptied into the duodenum and aid in the digestive process. The endocrine elements produce a secretion that enters the blood stream and is important in carbohydrate metabolism.

The pancreas is located in the upper part of the abdominal cavity, where it extends in a transverse plane from the loop of the duodenum, behind the stomach, to the spleen. It is divided into three portions: the *head,* which lies in the duodenal loop; a middle portion called the *body;* and the *tail* which lies in relation to the front of the left kidney. This organ does not have a distinct connective tissue capsule but is covered by a thin layer of loose connective tissue which is condensed on its surface, and from which connective tissue septa enter the substance of the organ to divide it into a number of primary and secondary lobules. The smaller division of the organ is known as the primary lobule. A number of primary lobules are grouped together by broader and more loosely arranged septa to form secondary lobules. In man the septa are often incomplete. The septa contain the ducts, blood and lymphatic vessels and nerves.

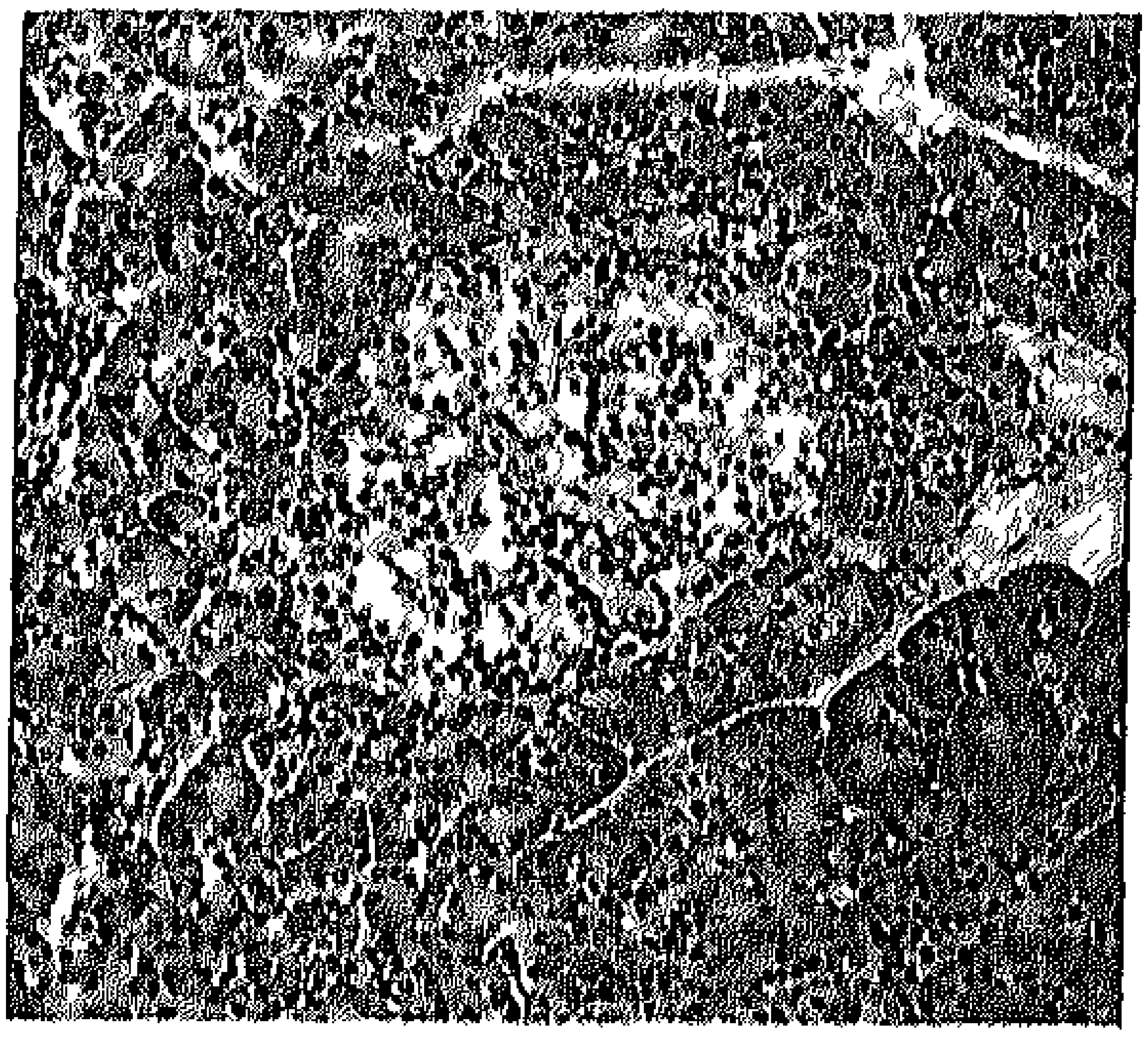


FIG. 154. Island of Langerhans (greatly magnified) surrounded by pancreatic tissue. Photomicrograph.

EXOCRINE PORTION. The exocrine portion of the gland consists of acinar- or alveolar-shaped secreting end pieces, together with a rather complex system of ducts organized as a compound tubuloacinar *(tubuloalveolar)* gland.

The cells which form the walls of the acinus (acinar cells) are pyramidal in shape. They show two rather distinct zones, an inner and a basal zone. The inner zone contains coarse, highly refractive, presecretory granules *(zymogen granules).* The quantity of these granules varies considerably, depending on the secretory stage of the organ.

Immediately following a meal, the number of these granules may be completely depleted, but during the resting stage the granules again appear, filling the inner zone and becoming so numerous that they even encroach upon the basal zone of the cell. The basal zone contains the nucleus and stains more deeply basophilic than the inner zone. It contains a basophilic substance which appears in the form of longitudinal striations or fine filaments. Very often it is seen merely as a homogeneously staining area. The exact significance of this basophilic substance is not known. It is not, however, a form of mitochondria as was once suggested. Mitochondria are present in the cell and a Golgi apparatus can be demonstrated. The nucleus is round and located in the basal portion of the cell. Its chromatin material is arranged in the form of a fine network. There may be one or more acidophilic staining nucleoli present. Very rarely, in man, are double nuclei present. Mitotic figures are seldom seen.

Extremely delicate canals (*intracellular canals*) have been described in the cytoplasm of the acinar cells. These canals communicate with other fine canals which extend between the cells (*intercellular canals*) and serve to convey the secretion to the lumen.

The cells of the acini rest on a definite, but thin, basement membrane.

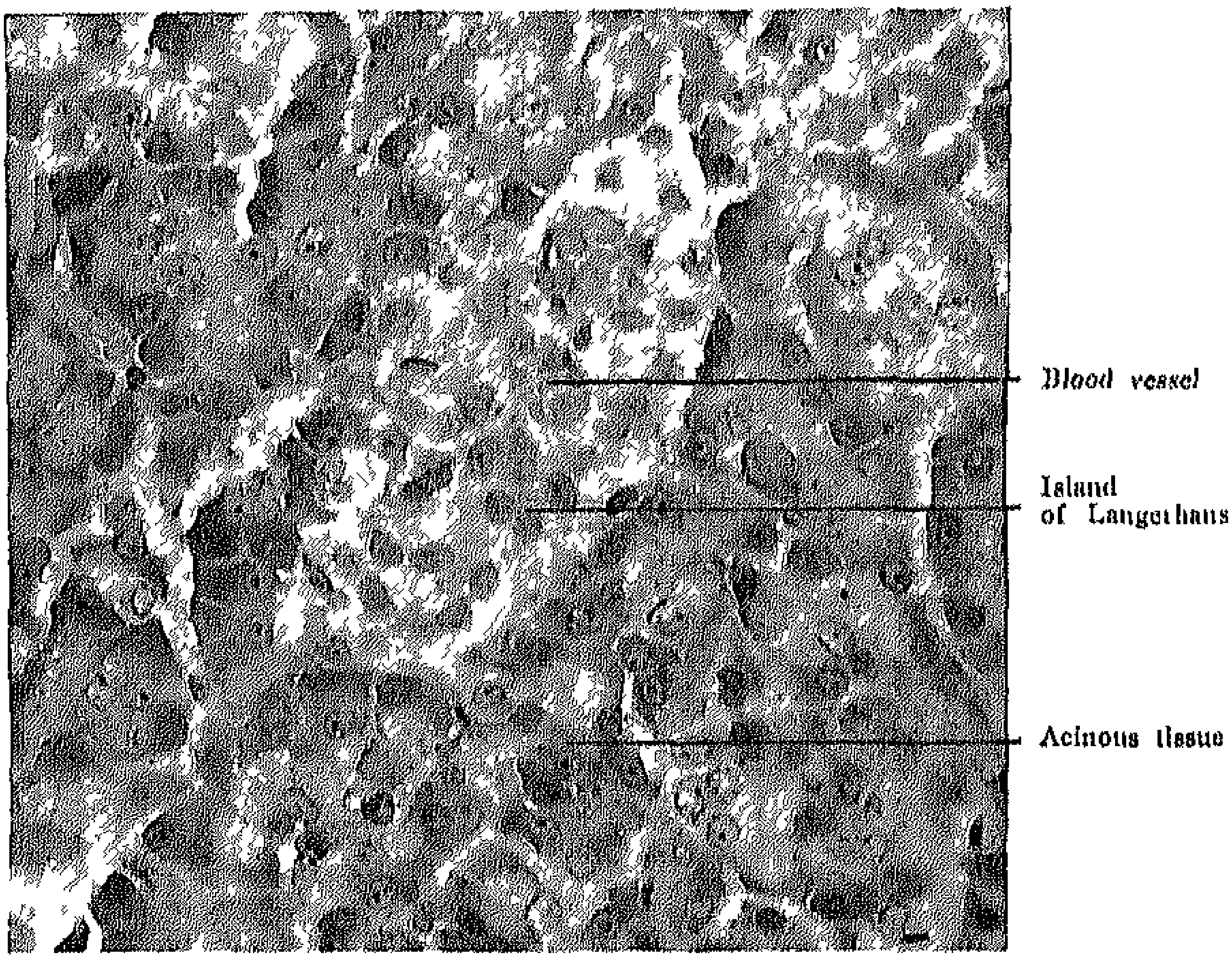


FIG. 155. Section of pancreas (cat) showing island of Langerhans with surrounding acinous tissue. Photomicrograph.

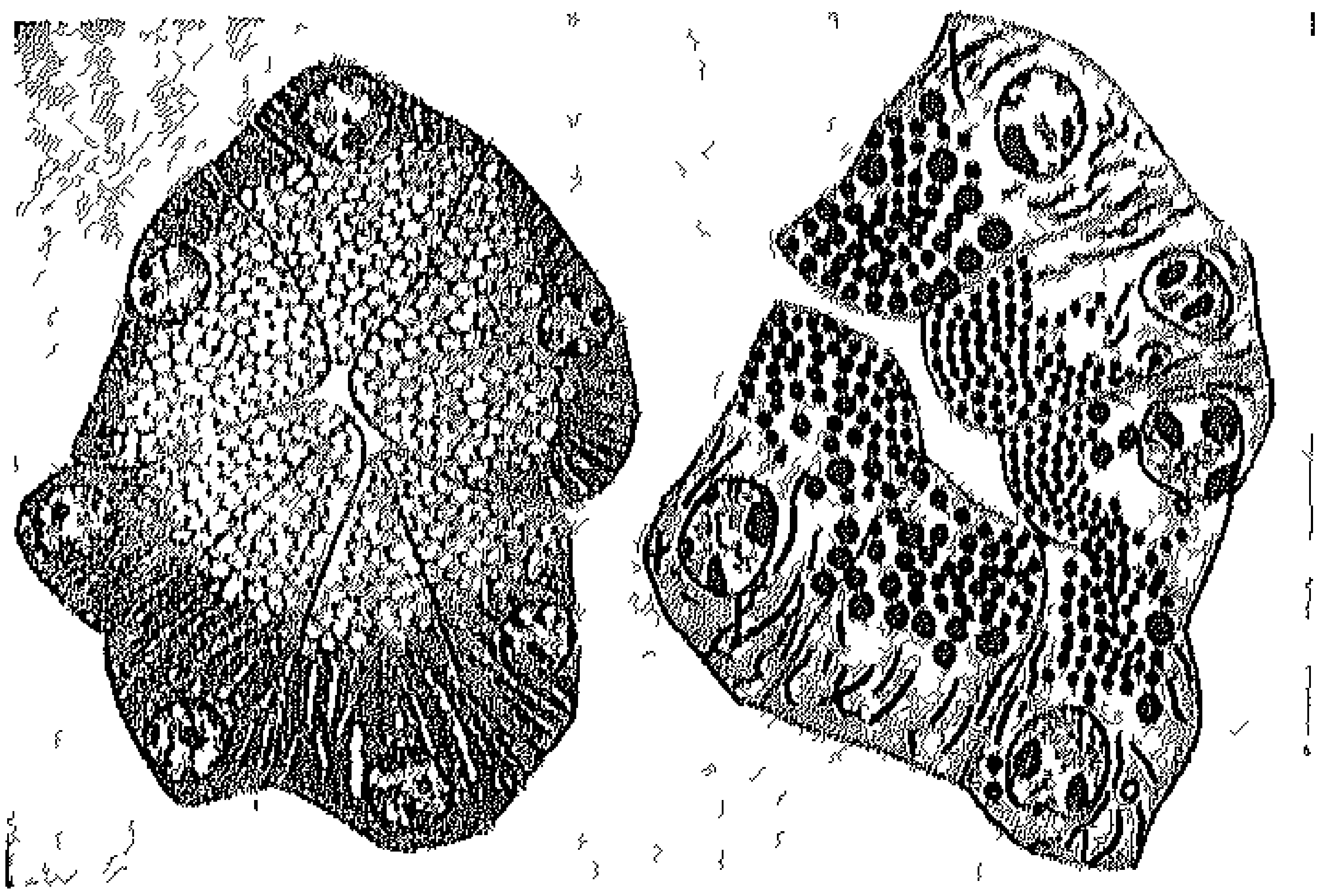


Fig. 156. Pancreatic acini (guinea pig). *(Left)* Note chromidial substance in basal zone. The unstained spaces in the apical zone represent zymogen granules and the unstained striations in the basal zone, mitochondria. Toluidine blue stain. (After Bensley, 1911.) *(Right)* Same tissue stained to show zymogen granules in apical zone and mitochondria in basal zone of cells. Acid fuchsin and methyl green stain. (After Bensley, 1911.) (Courtesy, Cowdry: "Special Cytology," New York, Paul B. Hoeber, Inc.)

Interposed between the apex of the acinar cells and the lumen is a layer of small, flattened epithelial cells known as *centroacinar cells.* The cytoplasm of these cells contains no granules and no basal striations can be demonstrated. The nuclei are oval and occupy the center of the cells. These cells are continuous with the epithelial cells of the intercalary ducts.

Beginning at the acinus, the duct system proper consists of: intercalary ducts, branches of the main duct, and the main duct itself (duct of Wirsung). In some cases an accessory duct (duct of Sartorini) may be present, and may open directly into the duodenum or it may join with the duct of Wirsung.

The intercalary duct is lined by a cuboidal epithelium. The point of junction with the centroacinar cells is sharp since the cells of the intercalary duct do not gradually diminish in height to become flattened like the centroacinar cells.

The branchings of the main duct are found in the septa between the primary and secondary lobules. The cells lining these ducts are cuboidal, becoming columnar as the diameter of the ducts increases.

The principal duct of the pancreas (duct of Wirsung) is lined by a simple columnar epithelium.

The epithelium of the ducts rests on a dense compact connective tissue which contains elastic fibers and longitudinal bundles of smooth muscle. As the diameters of the ducts increase, there is a corresponding increase in the thickness of their walls, due to an increase in the amount of the elastic and smooth muscle fibers. This is especially the case with the duct of Wirsung as it approaches the duodenum. In the ampulla of Vater, the smooth muscle in, and about, the duct is arranged in the form of a sphincter which keeps the aperture closed except when the secretion from the gland is being discharged.

ENDOCRINE PORTION. The *islands of Langerhans* represent the endocrine portion of the gland. They are made up of more or less spherical clusters of cells scattered among the acini. The islands vary greatly in size, the smallest may consist of only a few masses or cords of cells, while the largest are visible without the aid of a magnifier. They are relatively few in number in the head of the pancreas, somewhat more numerous in the body, and are most abundant in the tail.

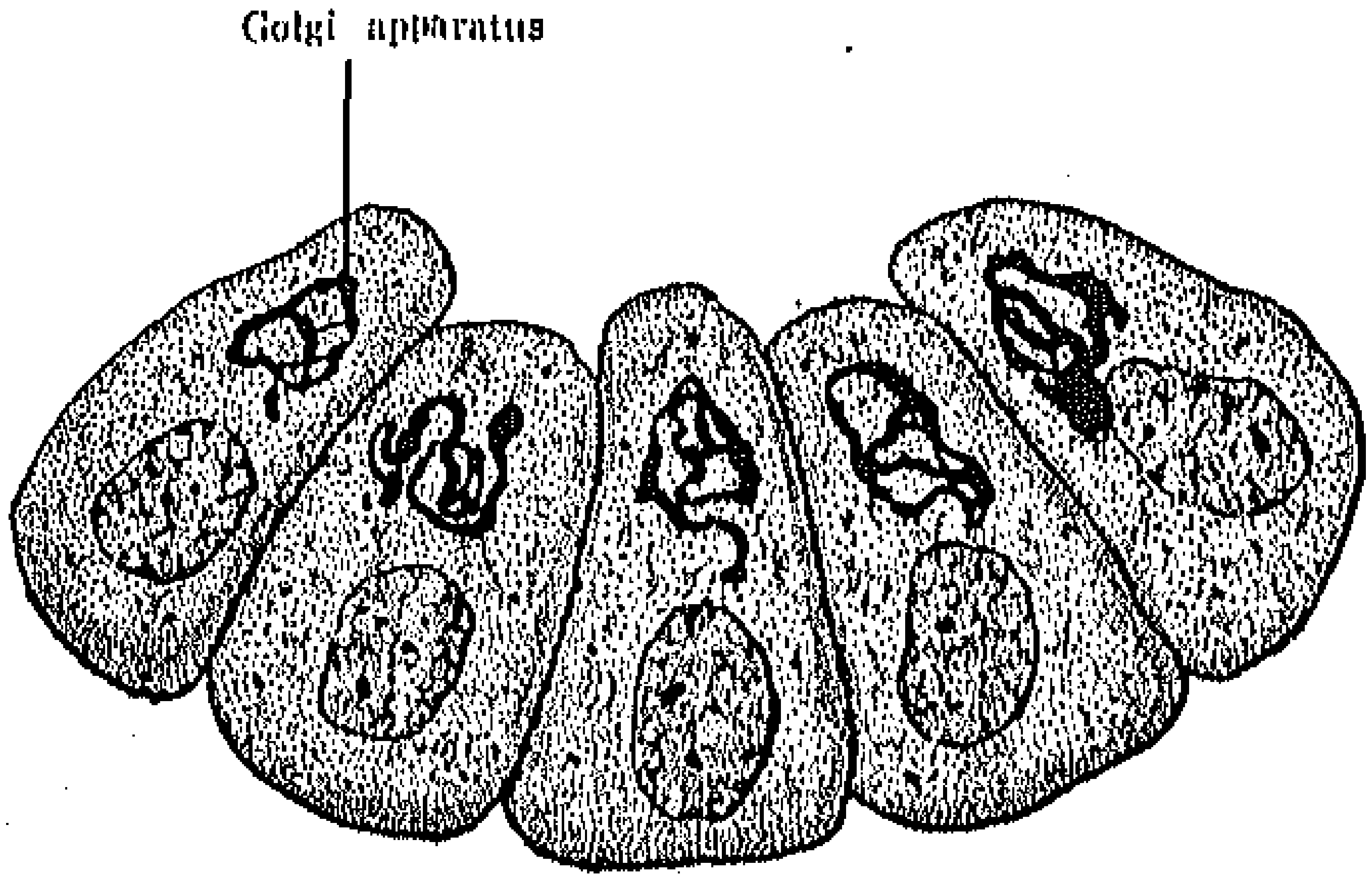
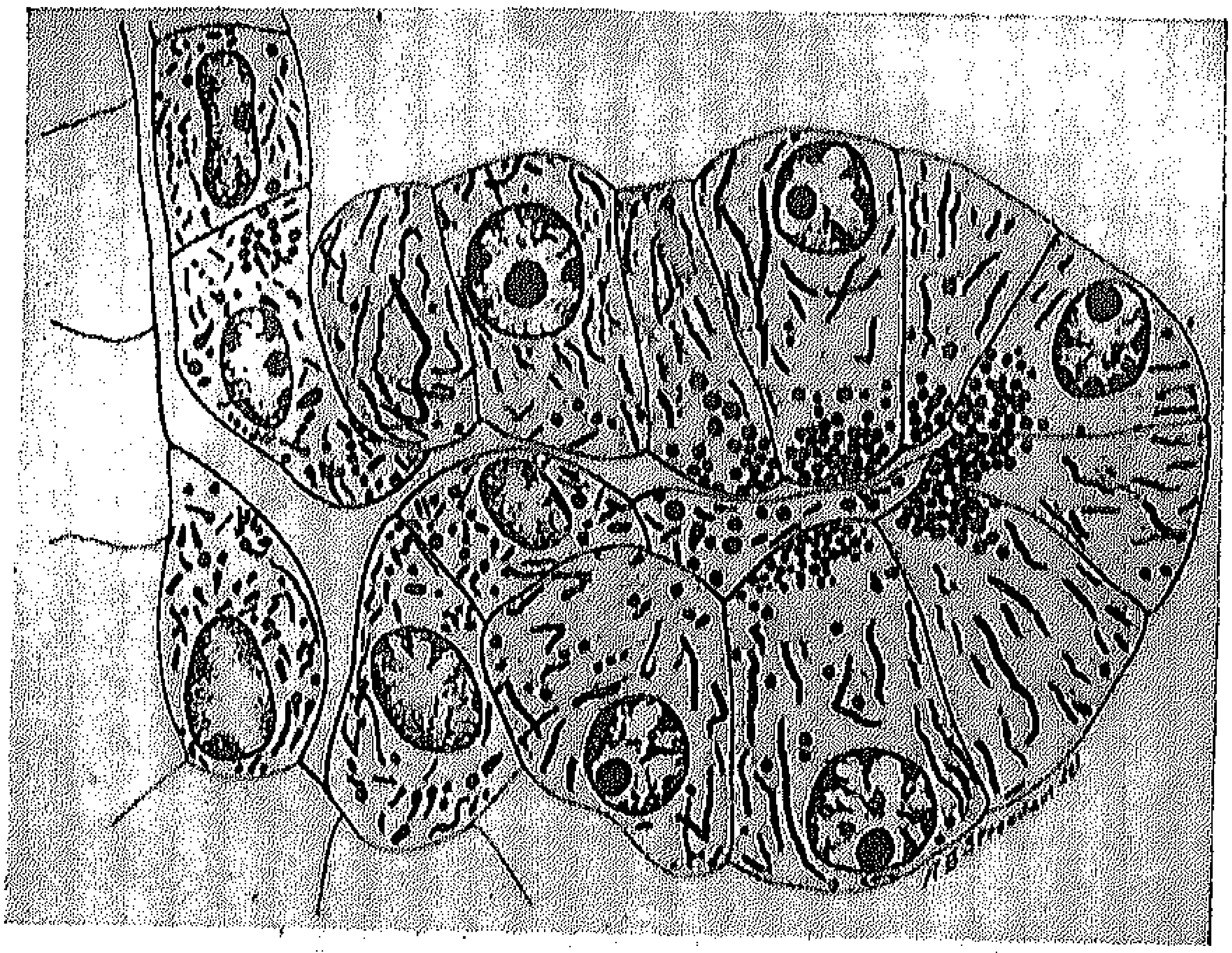


FIG. 157. Golgi apparatus in normal secreting cells of the pancreas.

In ordinary haematoxylin and eosin stained preparations the islands appear lighter than the tissue of the pancreas surrounding them. The cells forming the islands are arranged in irregular clusters or in the form of cell cords, which are in contact with thin-walled, sinusoidal capillaries. This close relationship between the cell cords and the sinusoids provides for a rapid transfer of the secretions of the cells to the blood stream.

By the use of special staining methods (Mallory or Masson stains) three types of cells can be distinguished in the islands of Langerhans of human pancreas. The first type, the A, or alpha cells, may be recognized by their large, oval nuclei which are poorly supplied with chromatin, and by the large, red staining granules which fill the cytoplasm. These granules are insoluble in alcohol. The cells of this type are fewer in number and show a greater tendency to aggregate in masses, than the cells of the second type. The B, or beta cells, differ from those of the



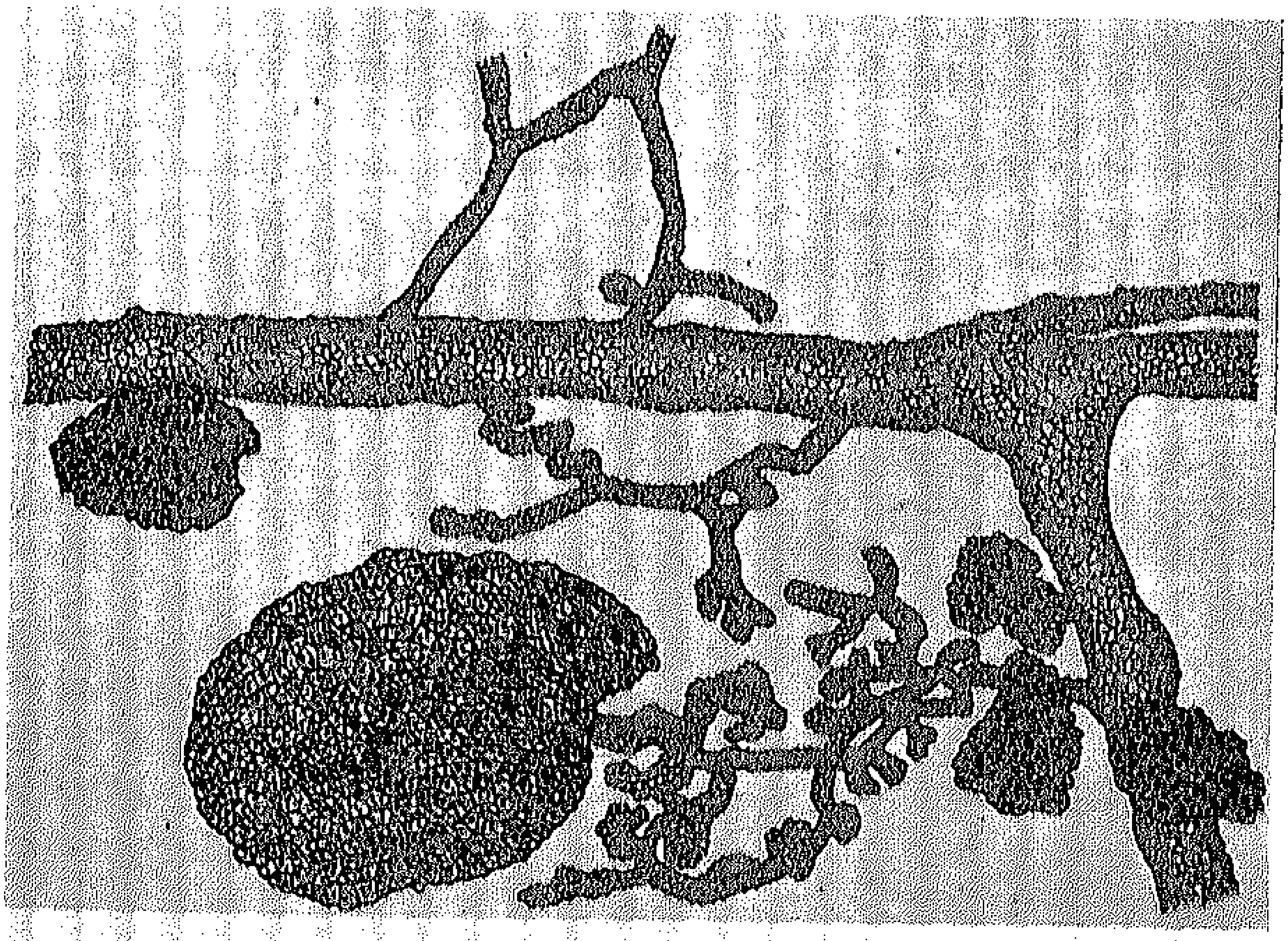


FIG. 158. *(Top)* Section of an acinus (guinea pig) showing centro-acinar cells with mitochondria and zymogen granules in the apical portion of the acinar cells. A portion of an intercalated duct is included. (After Bensley, 1911.) (Courtesy, Cowdry: "Special Cytology," New York, Paul B. Hoeber, Inc.)

FIG. 159. *(Bottom)* Duct with branches showing the highly branched tubules connecting the duct with an islet. (After Bensley, 1911.) (Courtesy, Cowdry: "Special Cytology," New York, Paul B. Hoeber, Inc.)

first type by the different staining reaction and chemical properties of their granules (granules are soluble in alcohol) and by the smaller, spherical nuclei which contain coarse chromatin masses. These are the most numerous of the island cells and are the type most commonly found in the cords. Type D cells are characterized by small, blue staining granules in their cytoplasm. These cells make up a very small percentage of the island cells. Another type of cell (type C) has been reported by Bensley as occurring in the pancreas of the guinea pig. The cytoplasm of this cell is free from granules.

The relation of the islands of Langerhans to the structure of the pancreas has been variously interpreted. Apart from the duct system for the exocrine portion of the pancreas, Bensley has described the presence of a system of small anastomosing tubules. These tubules are derived from the intralobular ducts and are found in the loose connective tissue septa around them. They do not carry secretions. These ducts are connected with the islands and occasionally with an acinus. The cells forming these tubules are low cuboidal; they have a homogeneous cytoplasm and the nucleus occasionally shows a mitotic figure. Bensley considers these cells to be undifferentiated cells which have the capacity for transforming into islet cells and possibly into acinar cells under certain conditions.

The pancreas produces two secretions: exocrine and endocrine. The exocrine secretion is produced by the acinar cells and is known as the *pancreatic juice*. It is alkaline in reaction and contains the enzymes trypsin, amylase and lipase. Trypsin is a proteolytic enzyme that forms amino acids from protein. Amylase breaks down starch into sugar and lipase is the fat-splitting enzyme. These enzymes, as such, do not exist in the acinar cells, where they would destroy the pancreatic tissue itself, but exist in the cells in the form of pro-enzyme substances. The acinar cells are activated by *secretin*, a hormone formed in the mucosa of the small intestine and reaching the acinar cells by way of the blood stream, or by *nerve impulses* through stimulation of the vagus nerve.

The endocrine secretion of the pancreas, produced by the islet cells, is *insulin*. This substance is essential for the proper regulation of the carbohydrate metabolism of the body. Commercial extracts of this material are used in treating and controlling diabetes.

THE LIVER

The liver is a very large glandular organ located beneath the diaphragm in the upper right side of the abdominal cavity. It consists of two large lobes: the right lobe, which makes up the right side of the organ, and the smaller left lobe which extends to the left, above and behind the stomach. Two smaller lobes are located on its inferior surface: the quadrate lobe, which is anterior in position, and the caudate lobe, which lies posterior. Except for a small area on its superior surface (the bare area), the surface of the liver is invested by an outer serous layer formed by the reflection of the abdominal peritoneum. Beneath this is a thin connective tissue layer containing a wealth of elastic tissue, which forms the capsule *(capsule of Glisson)*. The connective tissue of the capsule passes into the substance of the liver through a fissure on its inferior surface, the *hepatic porta*. Blood vessels and nerves also enter here and the connective tissue surrounds them and follows them, thus forming the supporting structure for the parenchyma *(hepatic cells)* and dividing the gland into its numerous small, irregularly arranged structural units, the *lobules*. In man the quantity of connective tissue surrounding the lobules is meager and in places incomplete, while in the pig the connective tissue surrounding the lobules is abundant and forms a thick investing layer.

The liver is peculiar in that its cells (hepatic cells) appear to be all alike cytologically, yet the organ carries on diverse functional activities. It functions as an exocrine gland in the production of bile which is excreted by way of ducts which ultimately transport the bile to the duodenum. Apparently these same hepatic cells store certain food substances (carbohydrates, proteins, fats) until they are needed by the body. Vitamins are also stored in the liver. One of the most important functions of the liver is its ability to act as a detoxicating agent of certain toxic substances in the body and the destruction of

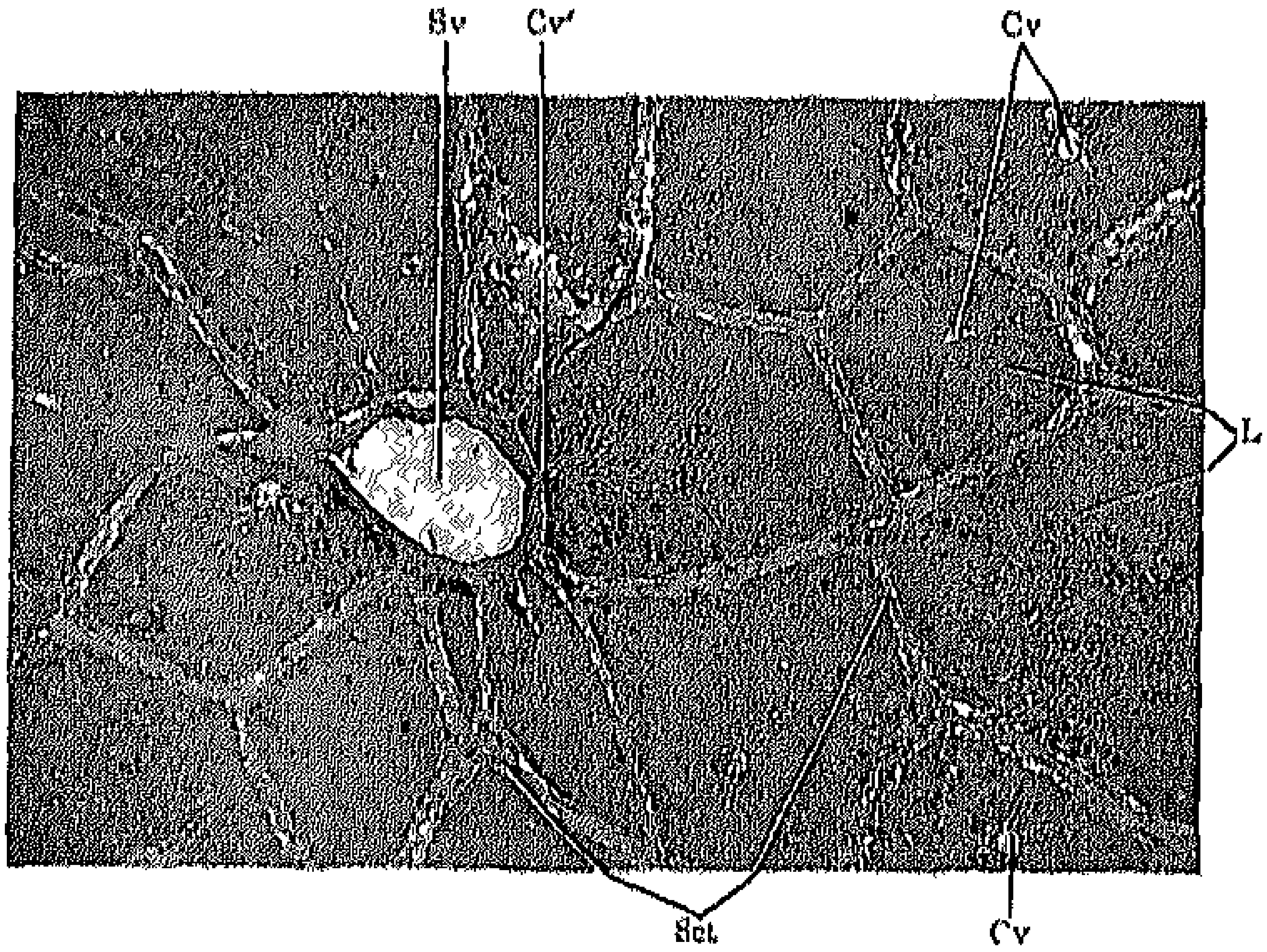


Fig. 160. Pig's liver. (Cv) Central veins. (L) Hepatic lobules. (Sct) Interlobular connective tissue. (Sv) Sublobular vein. The hepatic sinusoids are seen at Cv' converging on the central vein at the point where it opens into the sublobular vein. Photomicrograph.

foreign proteins involved in anaphylaxis. In a sense it also functions as a filter, screening out of the blood various foreign elements, including bacteria. The latter functions may be performed by the specialized cells of the reticulo-endothelial system which line the sinusoids between the hepatic cells. Other functions with which the liver seems to be intimately concerned are: coagulation of blood, iron metabolism and the maintenance of the fluid volume of the blood.

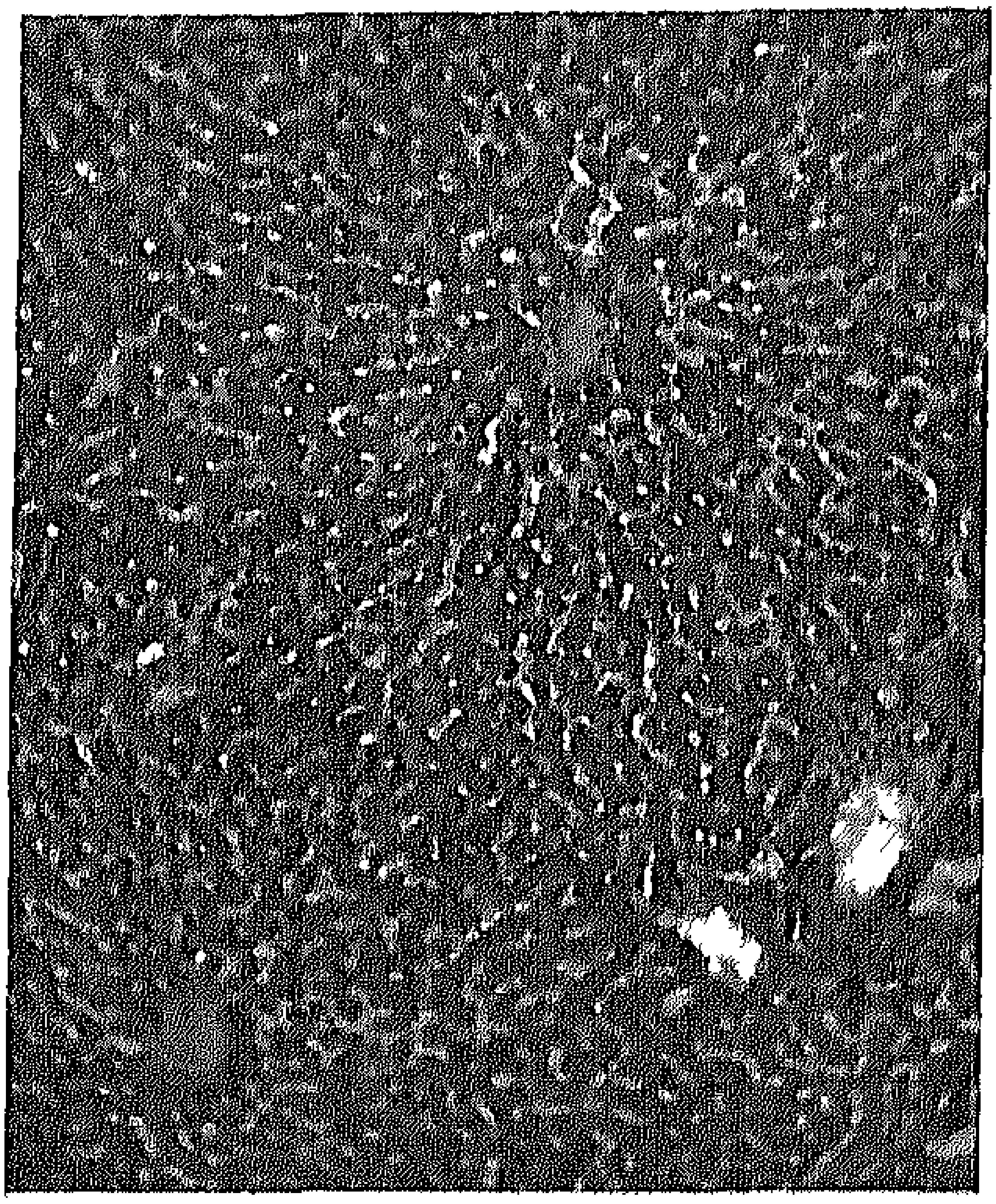


FIG. 161. Tangential section of human liver. The two central veins in cross section mark the centers of two lobules which are not sharply separated from each other by definite interlobular connective tissue septa. Photomicrograph.

Another peculiarity of the liver is the power it shows for regeneration, and the speed with which it occurs. One experimenter reported that he removed 70 per cent of the liver tissue from a dog and that within 48 hours, 75 per cent of the liver (by weight) was again present. However, the regeneration does seem to depend, at least to a large extent, on the portal circulation being intact. Whether hepatic cells, duct cells, or intermediate cells are responsible for forming the regenerating tissue is unknown.

THE BLOOD SUPPLY OF THE LIVER. Blood enters the liver

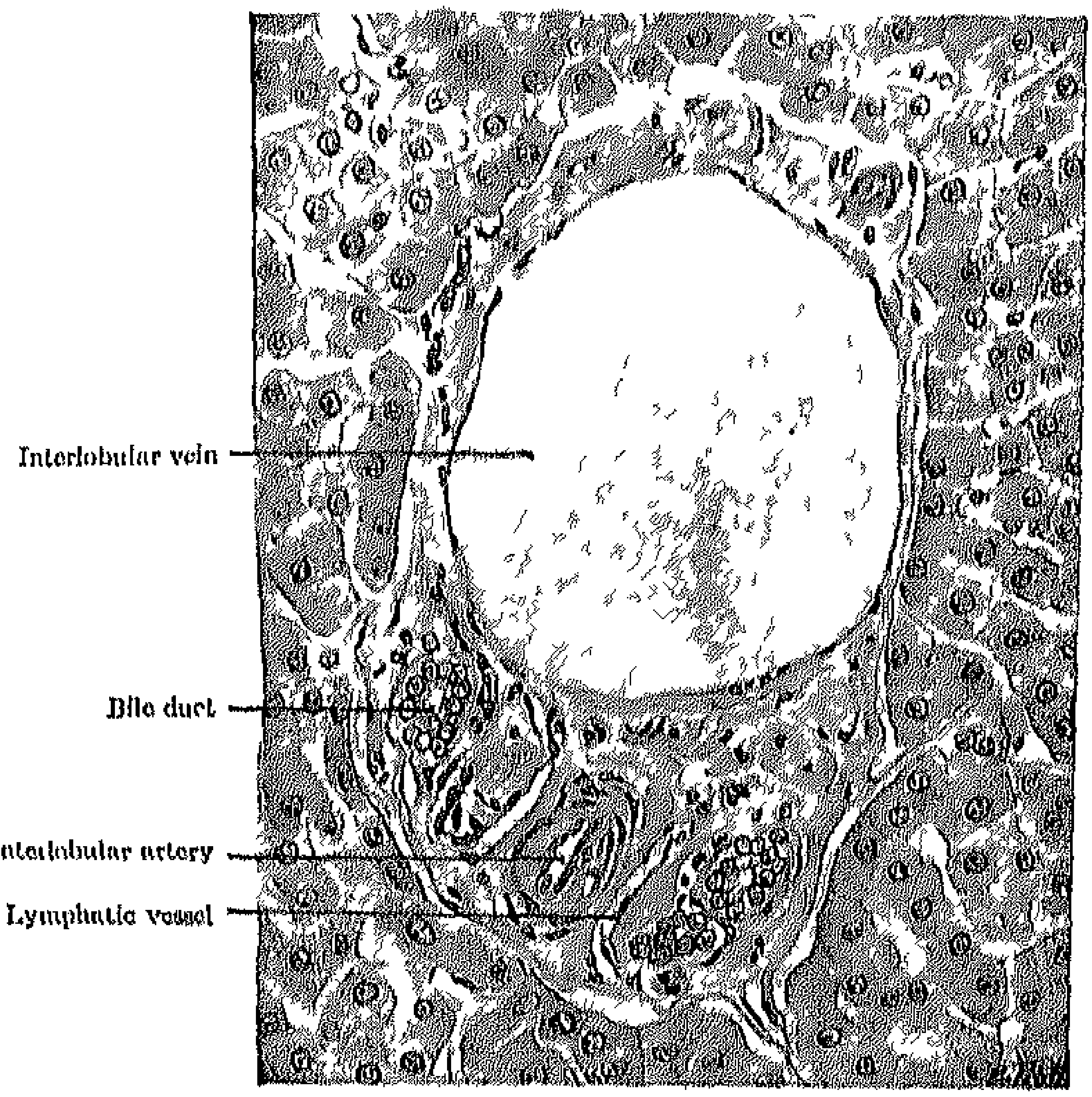


Fig. 182. Section through a portal canal in human liver. Hematoxylin and eosin stain (Courtesy, Bremer-Weatherford "Textbook of Histology," Philadelphia, The Blakiston Company.)

by two vessels, the *hepatic artery* and the *portal vein*. The artery is a branch of the coeliac axis and supplies the tissues of the liver with nutrient material and oxygen. The portal vein drains the blood from the intestines and the spleen. This blood contains substances derived from the digestion of foods which are to be stored in the hepatic cells, or are transformed by them into bile. The courses of these two systems of vessels through the organ is important and will be treated separately.

On entering the liver by way of the porta, both the hepatic artery and portal vein branch to form the *interlobar vessels* which course through the connective tissue septa between the lobes These vessels give off the *interlobular vessels* which form vascular plexuses around each lobule. The *capillary plexuses* of the hepatic artery drain either into the smaller interlobular divisions of the portal vein or may enter the lobule and terminate in the intralobular sinusoids of the portal system.

In its course through the liver the hepatic artery supplies the capsule by way of the capsular arteries and the coats of the vessels and ducts receive their blood from the vaginal arteries. The blood returns from these two areas by way of the hepatic veins which empty into the interlobular veins of the portal system. From the interlobular venous (portal) plexuses, branches are given off which extend into the lobules where they form the intralobular hepatic sinusoids. At this point, attention should be called to the fact that all the blood which enters the liver empties into the interlobular plexuses.

The sinusoidal vessels converge toward the center of each lobule where they empty into the *central veins* which represent the beginnings of the hepatic veins. At the base of the lobule the central vein joins with similar veins from neighboring lobules to form the *sublobular veins* which, in turn, unite to form the *hepatic veins*. These latter vessels converge on the posterior surface of the liver and enter the inferior vena cava as it lies in its fossa.

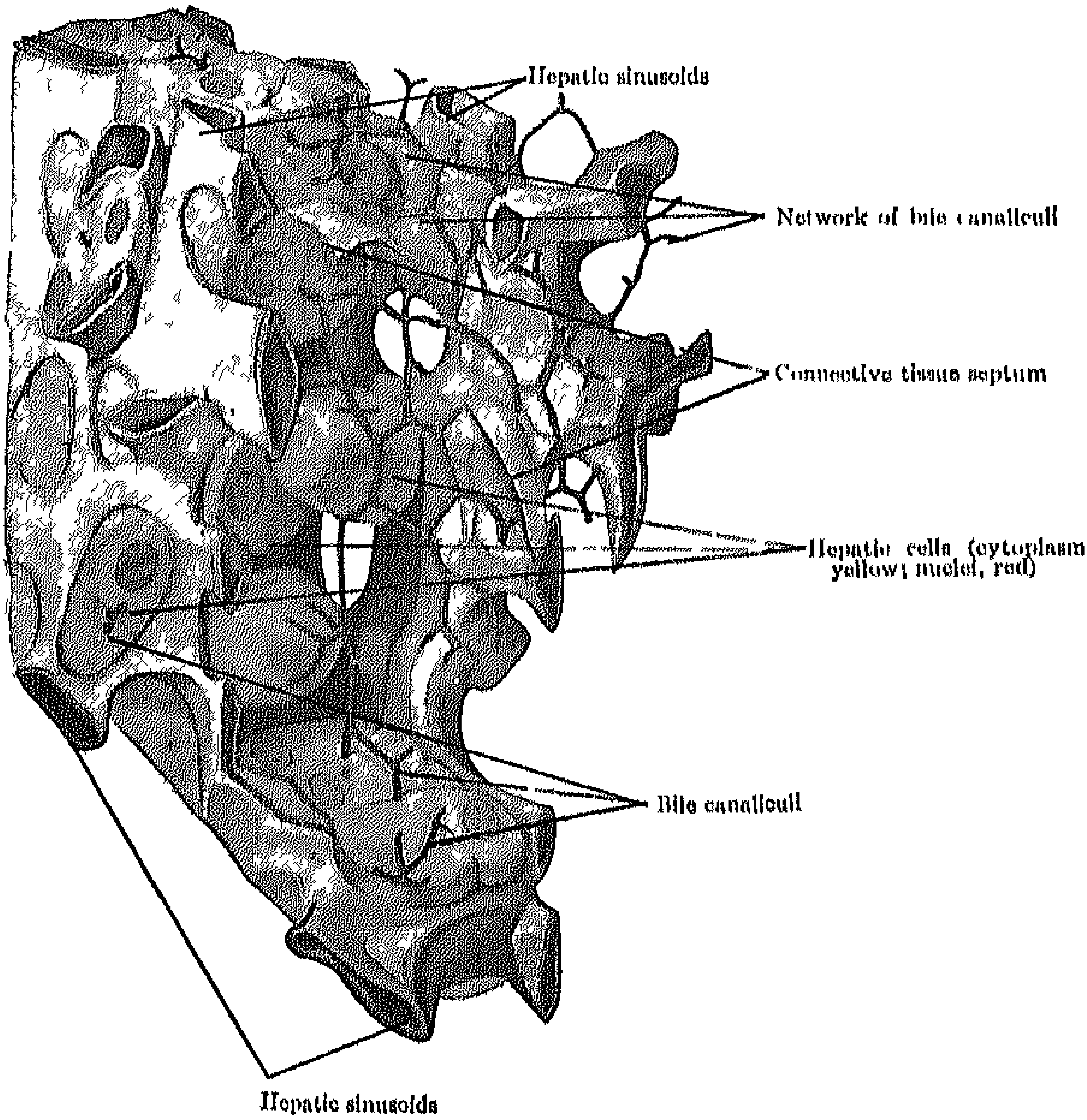


FIG. 168. Reconstruction of a portion of a liver lobule (human). Hepatic cell cords are yellow with red nuclei; hepatic sinusoids, blue; bile capillaries, green. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

THE BILIARY CANAL SYSTEM. The biliary system of canals for transporting bile starts as extremely fine *canaliculi* between the cords of hepatic cells in the center of the lobule. The walls of these canals are formed, supposedly, by the cell membranes of the adjacent hepatic cells. These canaliculi become larger as they extend away from the center of the lobule and at the periphery they empty into a series of small ducts *(ducts of Hering)* which join the *interlobular bile ducts.* The ducts unite and form larger and larger ducts which ultimately join to form the *right* and *left hepatic ducts* that leave the liver at the porta. After emerging from the liver these two vessels join to form the *common hepatic duct.* After its junction with the cystic duct from the gall bladder, the *common bile duct*, which empties into the duodenum, is formed.

The interlobular bile ducts are the smallest portion of the duct system to have an epithelial lining. These ducts are lined by a simple cuboidal epithelium which gradually increases in height until it becomes tall columnar in the larger ducts near the porta. The epithelium in the smaller ducts rests on a thin connective tissue layer which increases in thickness and contains elastic fibers and some smooth muscle fibers around the larger ducts. The extrahepatic ducts (hepatic, cystic, and common bile ducts), are lined by tall columnar cells with a scattering of goblet cells, which rest on a connective tissue stroma containing elastic fibers and smooth muscle. The stroma is raised into ridges, but it is not folded to form an alveolar surface. The quantity of smooth muscle varies in these ducts and within the common duct. The fibers of the muscularis are not arranged in definite layers, the longitudinal, oblique, and circular bundles being more or less interwoven with one another. In the lower end of the common bile duct the quantity of muscle increases, particularly those having a circular direction, and forms a sphincter muscle.

HEPATIC LOBULES. The liver is composed of a number of small, more or less cylindrical structures, the *hepatic lobules.* Portions of the fibrous capsule of Glisson, containing branches of the hepatic artery, the portal vein and the bile duct, are located between the lobules and are known as the *portal canals.* A large central vein occupies the central portion of each lobule.

Each lobule is composed of hepatic cells arranged in branching and anastomosing cords *(hepatic cords),* which radiate from the central vein to the periphery of the lobule. The spaces between the cords are occupied by the capillary sinusoids of the liver *(hepatic sinusoids).*

Each hepatic cord or trabecula is made up of two rows (rarely three) of hepatic cells. Between their contacting surfaces extend the bile capillaries, their walls being formed by the cell membrane of the hepatic cells. These bile capillaries possess lateral branches which form an anastomosing communicating network. The presence of bile capillaries can only be demonstrated by the use of special staining methods. The hepatic cords are made up of large, polyhedral cells (which in man range from 26-35 microns in diameter). They possess one, or frequently two, round centrally located nuclei which are poorly supplied with chromatin material. The nuclear membrane, however, is quite distinct. Acidophilic nucleoli are usually present and readily distinguished. The hepatic cell does not possess a true cell membrane, instead its place is taken by a condensation of the protoplasm at the surface of the cell. A Golgi apparatus is present, as well as mitochondria in the form of granules, rods or as a filament. Normally the mitochondria are paranuclear in position. Granules of carbohydrate material in the form of glycogen are present, as well as fat droplets, protein material and pigment granules. The quantity of any one of these inclusions, together with the internal structure of the cell, and therefore, the appearance of the hepatic cell, varies with the functional state of the organ.

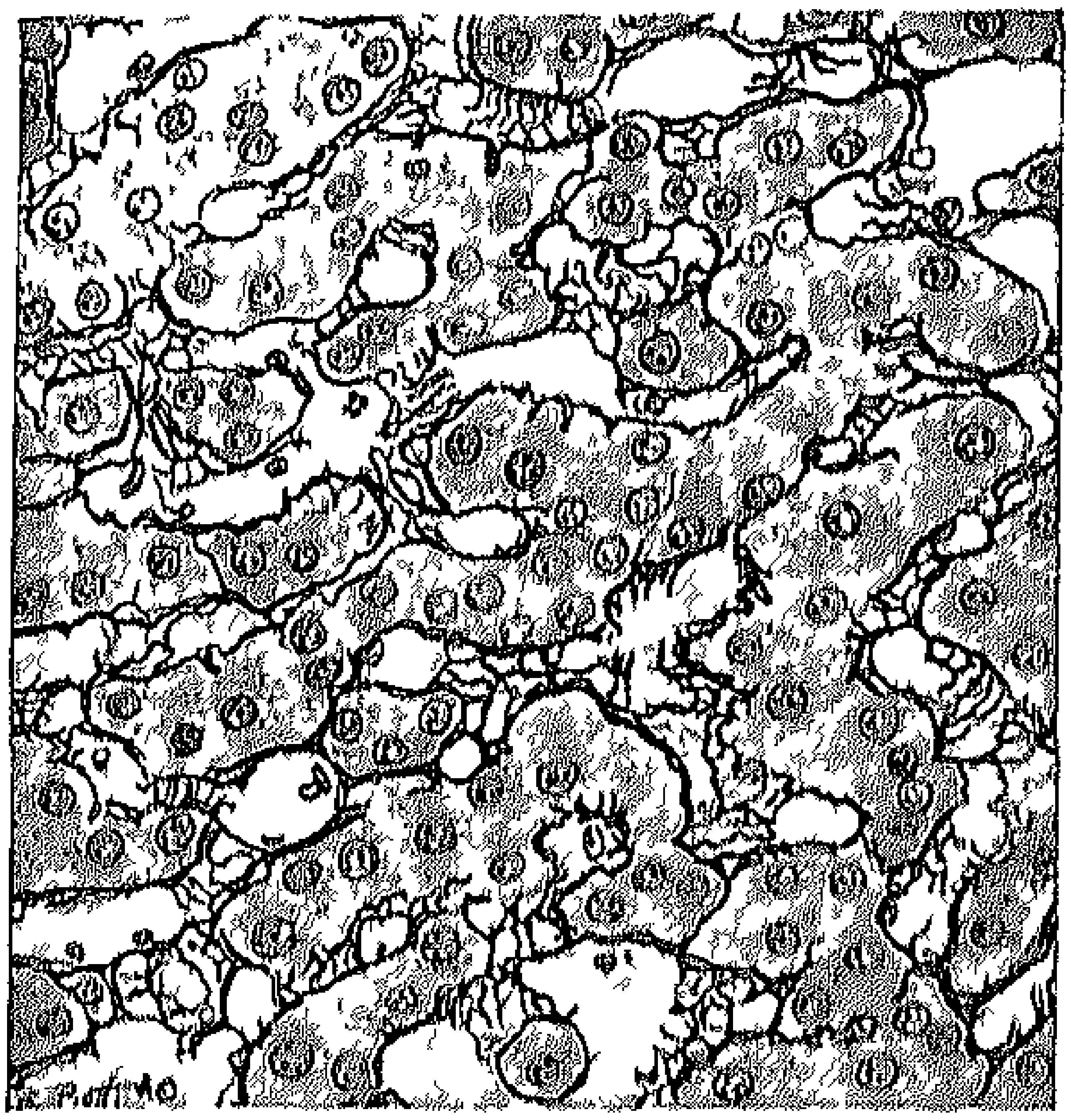


FIG. 164. Reticular fibers in relation to hepatic cells in human liver. Pap's method and hematoxylin. (Courtesy, Bremer-Weatherford: 'Textbook of Histology,' Philadelphia, The Blakiston Company.)

The hepatic sinusoids are thin-walled capillary structures which occupy the spaces between the hepatic cords. Two types of cells form a lining for the sinusoids. The cells of the first type are endothelial in character and are flat when viewed in profile, with small, deeply stain-

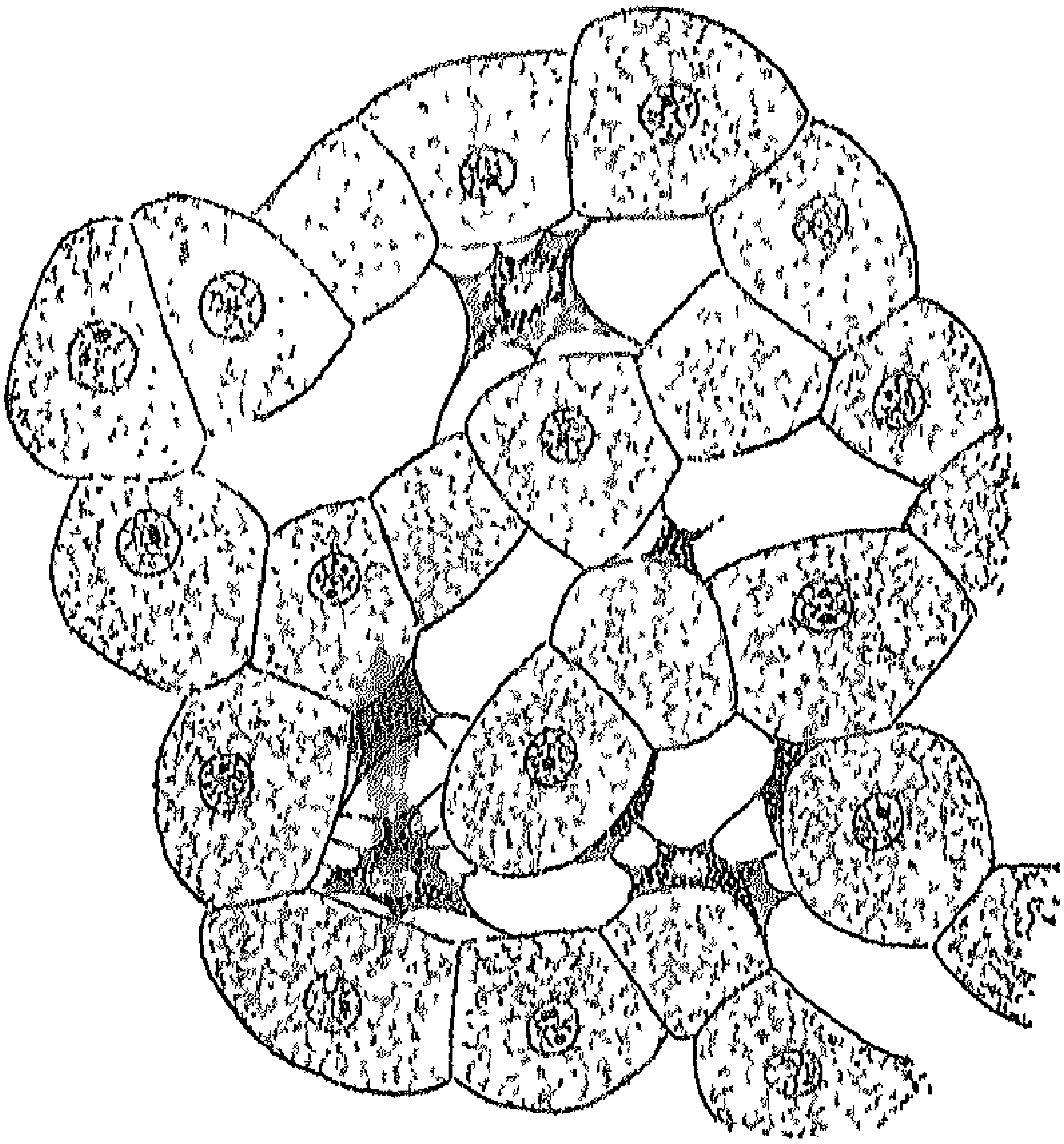


FIG. 105. Section of rat liver to show Küpffer cells in the hepatic sinusoids. The blue substance in the Küpffer cells is particles of injected trypan blue which had been injected intraperitoneally. (Courtesy, Smith and Copenhaver: "Bailey's Textbook of Histology," Baltimore, Williams & Wilkins Co.)

ing nuclei. They are not actively phagocytic. The cells of the second type are stellate in shape, and about half as broad as they are long. They are characterized by their large, centrally located, vesicular nuclei (they may have two nuclei) and by the fact that they are actively phagocytic. They are known as the stellate cells of Küpffer *(Küpffer cells)*. Unlike the other cells, they readily ingest particulate matter which has been injected into the blood stream. Because of this, their appearance varies with their activity. Normally the cytoplasm of these cells is homogeneous or finely granular, or it may be filled with ingested particles. When these cells become engorged with particulate matter that they have ingested, they assume a round form and are carried by the blood stream to the lungs where they are destroyed. In sections the cells may be seen stretching across the sinusoids.

The distribution of the lymphatics in the liver is not well understood.

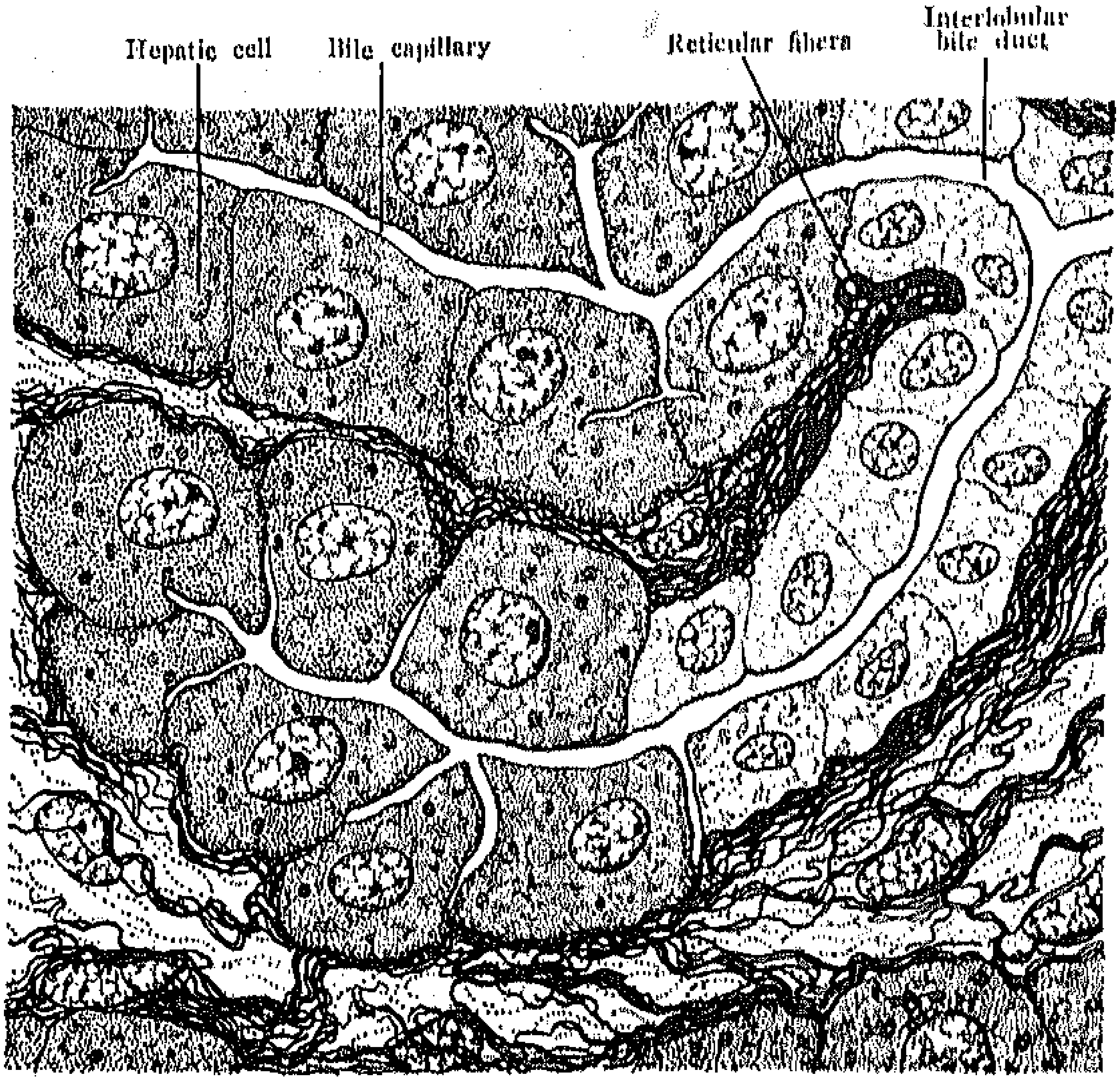


FIG. 166. Section through the margin of a hepatic lobule (human). Bielschowsky silver impregnation and Mallory-azan stain.

The nerves supplying the liver are mainly unmyelinated fibers from the autonomic system. They follow the extensions of the connective tissue of Glisson's capsule and end in the walls of the blood vessels and ducts. It is possible, but doubtful, that some of these fibers end in relation to the hepatic cells. A few myelinated fibers, which are probably sensory in function, have been traced into the interlobular connective tissue.

THE GALL BLADDER

The gall bladder is a pear-shaped sac which lies close to the anterior border of the liver, on its inferior surface. It functions as an adjunct to the liver, since it receives, concentrates and stores bile which is conveyed to it by the cystic duct.

Its wall consists of a *mucosa*, a *muscularis* and an adventitial layer *(adventitia)* of loosely arranged connective tissue by which it is attached to the surface of the liver. The mucosa is raised into a series of folds which are joined to one another by secondary folds. Both the primary and secondary folds are covered by extensions of the epithelium. When

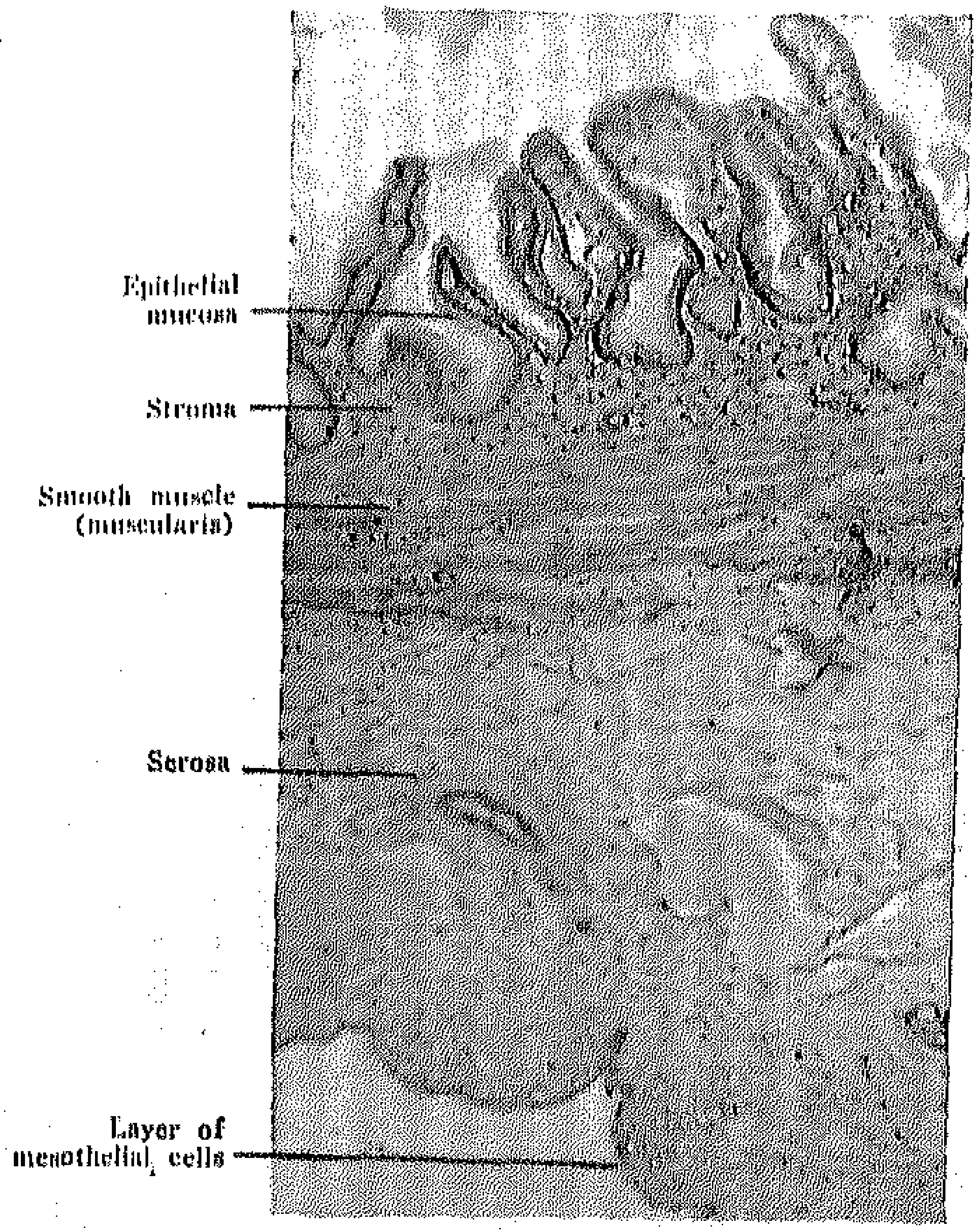


FIG. 167. Section through the wall of a gall bladder. Photomicrograph.

a mucous membrane is folded in this manner, it forms what is known as an *alveolar surface.* The folds are arranged so that they enclose pocketlike recesses which, in sections, have the appearance of glandular structures. These recesses are continuations of the lumen of the gall bladder. A portion of the hepatic capsule is carried over the surface of the gall bladder which is not adjacent to the surface of the liver, and forms the serosal layer.

The mucosa consists of an epithelium which rests on a subepithelial layer of delicate connective tissue, which has been called a "tunica propria" by some authors. However, there is no definite submucosa, the delicate collagenous and elastic fibers of the subepithelial layer extend from the epithelium to the muscularis, for which reason it should be more properly designated as a *stroma.* The epithelium consists of tall columnar cells, which are not unlike those found in the lining of the intestinal canal. Goblet cells have been described as occurring in the epithelium, and it is also claimed that the columnar cells possess striated borders. Both of these observations have been denied. However, it has been demonstrated, by the use of selective stains, that the epithelial cells produce a mucoid substance which first appears in the form of small droplets, the droplets coalescing to form a more or less homogeneous mass of mucoid material with which the cells may be filled. The suggestion has been made that the striated appearance at the free borders of the cells is due to the fine streams formed by this mucoid material as it passes from the cell. This view is supported by the mucoid reaction of the striae when selective stains are used. It is probable that the substance produced by these cells is added to the bile giving it its mucoid consistency. It is also possible that the cells are active in removing the excess of water from the bile by absorption. Glands are not present in the wall of the gall bladder, but small glands of the tubuloacinar type are to be found close to its junction with the cystic duct.

Small glandlike outpocketings of the epithelium are sometimes found extending through the stroma and muscularis. They connect with the lumen of the gall bladder and are known as *Rokitansky-Aschoff sinuses.* Their presence is thought to be due to abnormal conditions of the wall of the gall bladder allowing the mucosa to "rupture" through the muscular layer. Other epithelial lined spaces are found in the wall of the gall bladder (particularly on the side adjacent to the liver). These are blind tubules that have no opening into the lumen of the gall bladder and are thought to be remnants of fetal structures (biliary ducts). They are known as the true *ducts* of *Luschka.*

The muscular layer, which consists of longitudinal, oblique, and circular fibers, lies external to the stroma. The longitudinal fibers adjacent to the stroma form a more or less definite layer. The oblique and circular fibers are intermingled and do not form definite layers.

The wall of the gall bladder is completed by a thin layer of closely interwoven connective tissue fibers which lies upon the muscular layer. External to this is a layer of loosely arranged fibrous tissue by which the gall bladder is attached to the surface of the liver. The surface which is not directed toward the liver is covered by a serous membrane.

STRUCTURAL CHARACTERISTICS OF GLANDS ASSOCIATED WITH THE DIGESTIVE TRACT

	Type	*Type of Acini*	*Duct System*				*Name of Main Duct*
			Intercalary	*Intralobular*	*Interlobular*	*Interlobar*	
Submaxillary	Compound branched tubuloacinar	Predominately serous Few mucous Some serous demilunes	Present, relatively long	Present	Present	Present	Wharton's
Sublingual	Compound branched tubuloacinar	Mucous acini predominate Very few serous acini Very few serous demilunes	Absent	Present	Present	Present	Several terminal ducts
Parotid	Compound branched tubuloacinar	Serous Occasional mucous acini	Present, relatively long	Present	Present	Present	Stensen's
Pancreas Exocrine portion	Compound branched tubuloacinar (both alveolar and acinar end pieces)	Serous	Present, long and narrow	Present	Present	None	Wirsung
Endocrine portion	Cell cords or irregular masses of cells	None	No ducts				
Liver	Compound tubular	Cords of cells	None	Present	Present	None Place taken by right and left hepatic ducts	Common hepatic duct

16

The Respiratory System

The respiratory system includes the *lungs* and a number of connecting passages leading from them to the exterior. These passages serve to direct air into the lungs where it is brought into relation with the blood for the exchange of oxygen and carbon dioxide. Listed in order from the lungs, these passages are: *bronchi, trachea, larynx, nasopharynx* and the *nasal fossae.*

NASAL FOSSAE

In passing into the respiratory tract the air enters through the nose (the mouth being closed in the ordinary method of breathing). The nasal chamber is divided into lateral halves *(nasal cavities; nasal fossae)* by the median nasal septum, a membranous partition supported by bone and cartilage. Three curved processes called *conchae* project from the lateral walls of the fossae. Each lateral cavity *(fossa)* presents three regions: a lower region, the *vestibule;* a middle or *respiratory* region; and an upper or *olfactory* region. The first part, or vestibule, lies within the flare of the nose. Its walls are formed by the nasal wings *(alae)* which are supported by plates of cartilage. The vestibule extends for only a short distance from the external openings of the nose *(nares).* It is lined by a relatively thick layer of stratified squamous epithelium (the continuation of the epidermis of the skin), which gradually changes as it nears the middle of the vestibule to a stratified squamous minus the cornified layer of cells. This in turn merges with the respiratory epithelium of the respiratory area. The epithelium rests on a stroma of areolar connective tissue, from which a number of papillae extend into its deeper surface. The outer part of the vestibule contains a number of coarse hairs *(vibrissae)* with which are associated sebaceous and sweat glands. In the inner part of the vestibule these glands are replaced by muco-serous glands.

The respiratory region is the most extensive of the three areas into which the nasal fossae are divided. It is lined by a mucous membrane *(Schneiderian membrane)* which covers the surfaces of the inferior conchae, the greater part of the surfaces of the middle conchae, and the corresponding surface of the nasal septum. The mucous membrane consists of pseudostratified, ciliated epithelium which rests on a well-defined basement membrane. Between the basement membrane and the bone is a stroma of areolar tissue. Goblet cells are present among the columnar epithelial cells where they frequently occur in groups, which form the lining of depressed, pitlike areas known as the *mucous crypts*. Considerable variation in the form of the epithelium may be expected, from simple columnar on the under surfaces of the conchae to pseudostratified epithelium on their upper surfaces, and even stratified squamous which appears when the pseudostratified epithelium has been exposed to an intense or prolonged irritation.

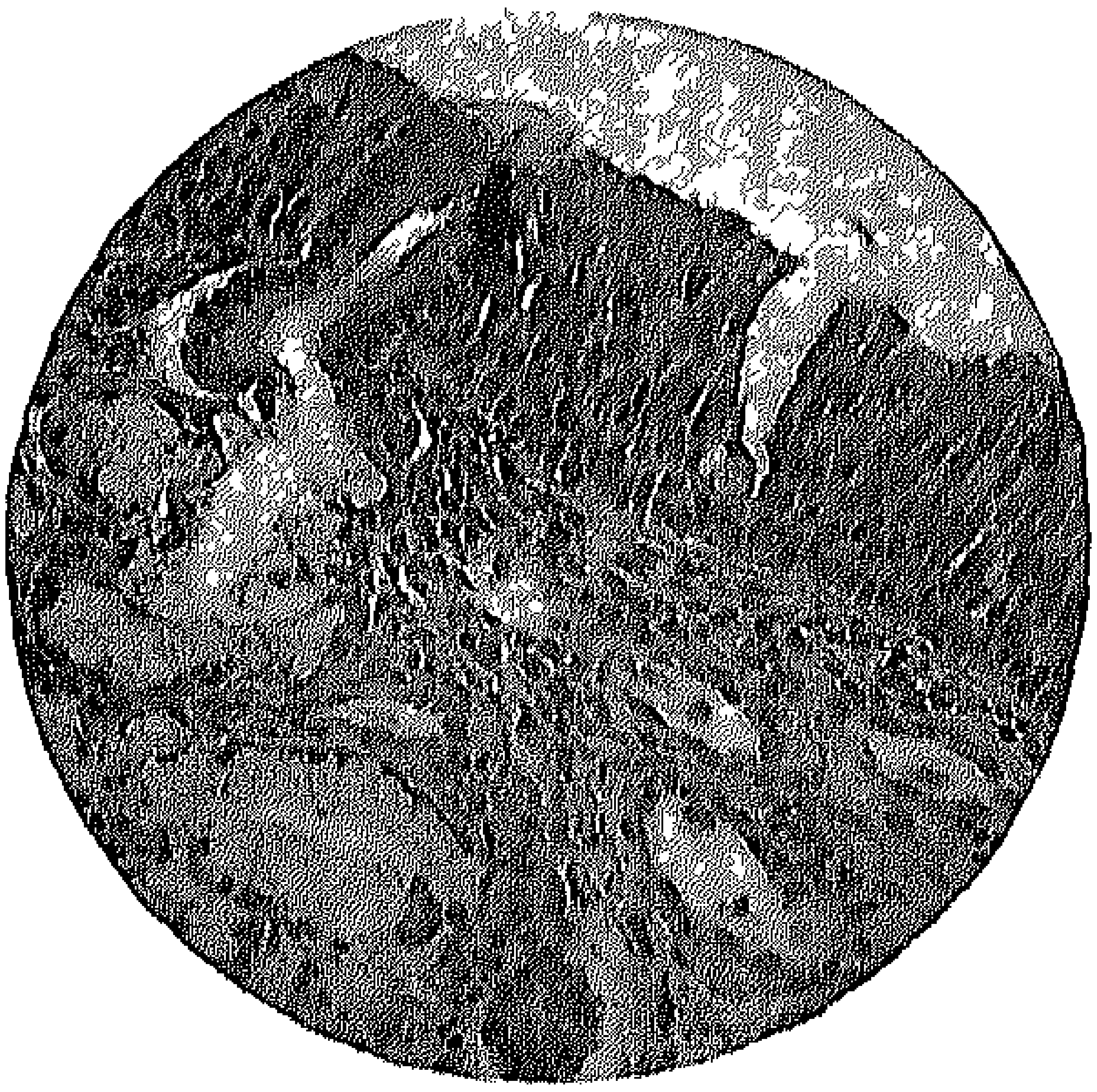


FIG. 108. Respiratory mucosa of the nose. The duct on the left is lined with ciliated epithelium. The alveolar end piece of a mucous gland is seen in lower left. Photomicrograph. (Courtesy, Proetz: "Applied Physiology of the Nose," St. Louis, Mo., Annals Publishing Co.)

The collagenous and elastic fibers of the stroma are loosely interwoven immediately beneath the epithelium, but are condensed toward the bone where they are merged, finally, with the periosteum. The stroma varies in thickness in the various parts of the respiratory region. It is quite thick over the inferior concha, but is considerably thinner over the corresponding area of the median septum. Numerous thin-walled veins are found in the regions of the inferior and middle conchae and the nasal septum just opposite. These venous structures are capable of being greatly distended and give the stroma an appearance not unlike that of erectile tissue. Tissues in which this form of vascularization appears are sometimes referred to as *false erectile tissue*, and differ from true erectile tissue in having no muscle fibers in the connective tissue trabeculae supporting the veins. The mucous membrane of the respiratory region is very vascular and this gives it a deep red color. When the vessels are filled with blood, the warmth of the membrane is increased and serves to warm the inhaled air. A number of mixed serous and mucous glands of the tubuloacinar type are present in the stroma. Their secretion serves to protect the epithelium from the drying action of the air.

The olfactory region is confined to the roof and the upper part of the sides of the nasal fossae. On the lateral side it may extend downward as far as the upper surface of the middle concha, while on the median side its downward extent on the nasal septum may be a half inch or less. *Owing to the presence of a pigment in its epithelial cells,*

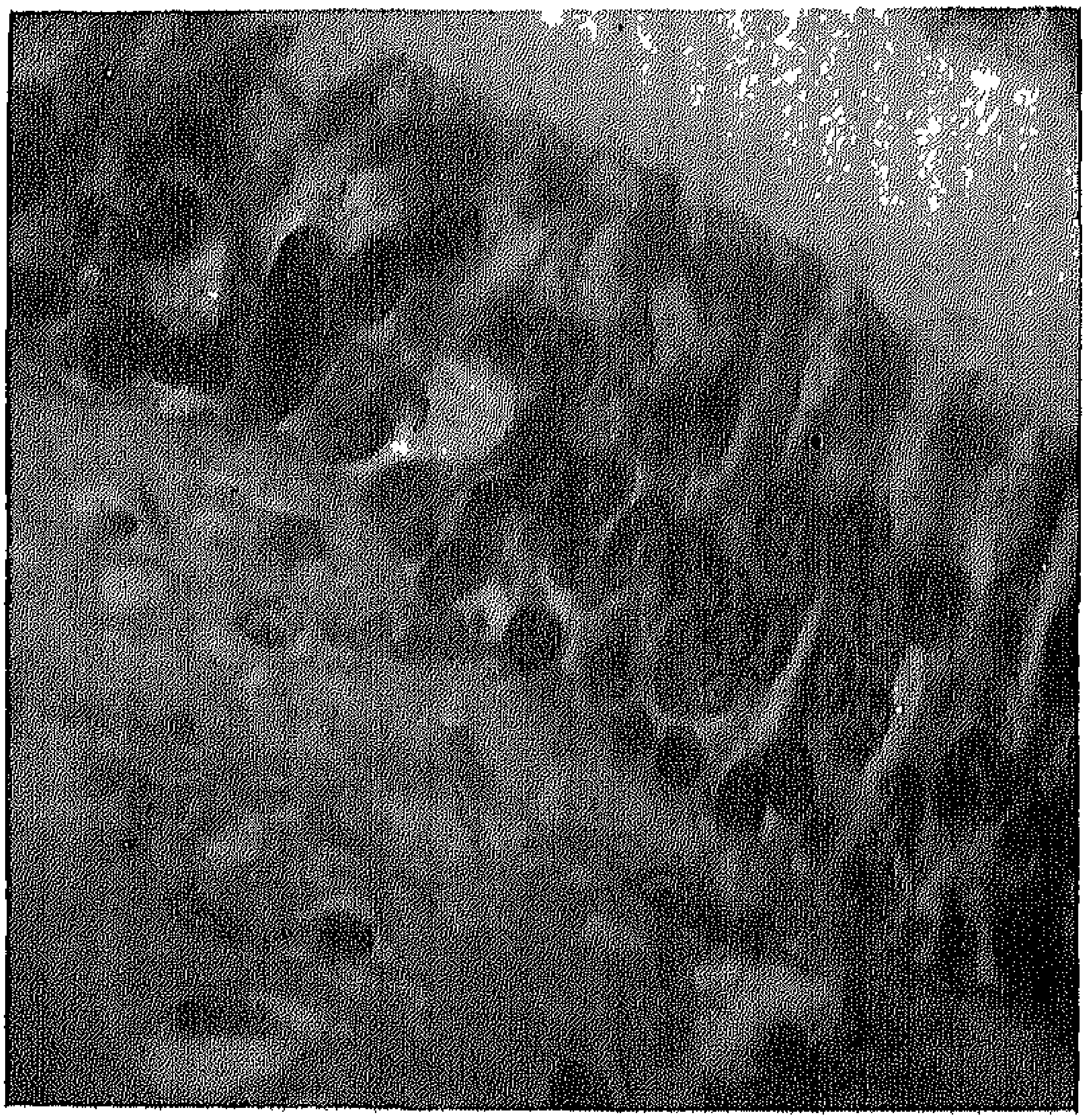


FIG. 169 Ciliated epithelium of the respiratory region of the nose. Photomicrograph. (Courtesy, Proetz: "Applied Physiology of the Nose," St. Louis, Mo., Annals Publishing Co.)

the olfactory region can be recognized grossly by its brownish yellow color, which contrasts sharply with the red of the respiratory region. The olfactory mucous membrane consists of a pseudostratified epithelium which, unlike the epithelium of the respiratory region, is not provided with a basement membrane. Beneath the epithelium is a stroma of loosely interwoven collagenous and elastic fibers which blends with the periosteum in its deep portion.

Three kinds of cells are present in the olfactory epithelium: the supporting *(sustentacular)* cells, the sensory *(olfactory)* cells, and the *basal* cells.

The sustentacular cells are the most numerous. Each cell presents two distinct areas: a tall, cylindrical, nonciliated superficial portion and a long, slender, forked basal portion. The superficial portion contains granules arranged in longitudinal rows and a yellow pigment which gives the epithelium its characteristic color. The free surfaces of these cells are provided with cuticular borders or plates which are joined together by terminal bars. The nucleus is oval in outline and is located in approximately the middle of the cell, where it first expands to form the superficial portion. The oval nuclei of these cells occupy the same plane and form a single row which is called the "zone of oval nuclei." The slender, basal portion is marked by indentations produced by the pressure of the vesicular portions of the olfactory cells. These forked processes extending from the base of the cell anastomose with similar processes from other cells and in the absence of a basement membrane they interlace with the fibers of the adjacent portions of the stroma, thus anchoring the epithelium to the underlying tissue. Between the basal processes are located the basal cells. Occasionally ciliated cells are seen among the olfactory cells and they represent areas of respiratory epithelium that have invaded the olfactory area.

The olfactory cells are interspersed among the sustentacular cells. Structurally these cells are actually bipolar ganglion cells and are first order neurons. The olfactory cells consist of an enlarged basal portion, the *olfactory vesicle*, in which the spherical nucleus is located. The nuclei of the olfactory cells are located at varying levels (below the oval nuclei of the sustentacular cells) and form an area known as the "zone of round nuclei." A slender protoplasmic process extends from the vesicle to the surface of the epithelium where it ends in a number of hairlike processes, the *olfactory hairs*, which reach the surface by passing through perforations in the cuticular plate. A delicate, fiberlike process extends from the vesicular, basal portion of the cell in the opposite direction. This joins with a number of similar processes from the other olfactory cells to form the *filia* of the olfactory nerve. The bundles formed by these fibers pass through perforations in the cribriform plate of the ethmoid bone and end in the olfactory

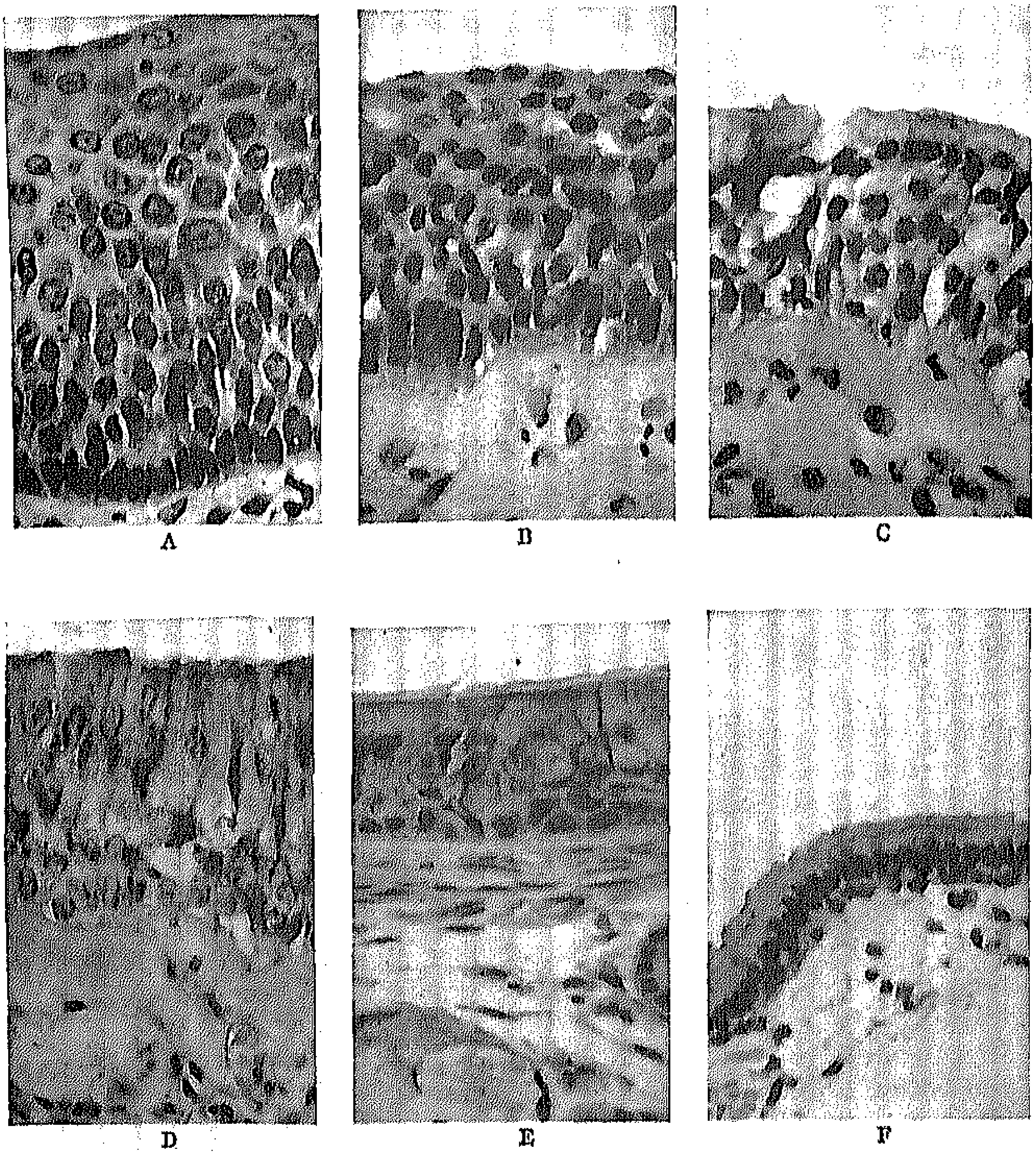


FIG. 170. Regional differences in nasal epithelium. (A) Preturbinal region close to the anterior end of the middle meatus. (B) Anterior third of the inferior turbinate. (C) Transitional form of epithelium from posterior portion of anterior third of the inferior turbinate. (D) High columnar epithelium from the middle third of the inferior turbinate (type common to most surfaces of the common meatus). (E) Epithelium from middle meatus. (F) Entire thickness of the mucous membrane from the frontal sinus of the dog. (From Anderson Hilding, *Arch. Otolaryng.*, XVI, 1932, with permission of American Medical Association.)

bulb. The olfactory cells may be regarded as bipolar ganglion cells located outside the nervous system. The enlarged, vesicular portion constitutes the cell body. The process which extends from the cell body to the surface of the epithelium is the dendrite, while the long, slender, basal process is the axon.

The third type of cell in the olfactory epithelium is a small, stellate-shaped cell located between the basal processes of the supporting cells. Their cytoplasm contains fine granules and may contain pigment granules. The nucleus is small, oval and deeply staining. They form the deepest zone of nuclei. The protoplasmic branches of these cells anastomose with similar branches from other basal cells, and also with the basal processes of the supporting cells. This network of processes forms a supporting reticulum for the epithelium, through which the fibrous processes (axons) of the olfactory cells may pass. This reticulum takes the place of a basement membrane.

The stroma consists of loosely interwoven collagenous and elastic fibers, which give support to numerous blood vessels and lymphatics. In addition, it contains a number of branched tubular glands *(olfactory glands of Bowman)* whose secretory portions consist of large pyramidal or columnar cells similar in appearance to serous cells. The excretory portion of the gland (the duct) is lined with a simple low cuboidal epithelium. These glands produce a serous secretion that serves to keep the surface of the epithelium moist and, at the same time, aids in the reception of olfactory stimuli. The basal processes of the olfactory cells, which enter into the formation of the olfactory nerve, occupy a zone between the epithelium and the stroma. The more loosely arranged portions of the stroma contain a number of scattered lymphocytes, which occasionally form diffuse aggregations, especially in the part of the membrane that lies near the passage from the nasal fossae to the naso-pharynx. In those parts of the membrane where lymphoid tissue is most abundant, lymphocytes may be seen passing between the cells of the epithelium to its surface.

A tubular invagination of the epithelium is sometimes to be found in the lower part of the nasal septum. This invagination, which extends backward and ends as a blind sac in the mucous membrane, is known as *Jacobson's organ.* It is found in the lower animals, especially those which possess a keen sense of smell. It is present in the human fetus and early infant, but only occasionally persists to adult life. The epithelium on the medial wall of the invagination consists of cells similar to those which line the respiratory region of the nasal fossa. Jacobson's organ is regarded as a rudimentary (vestigial) organ of olfactory sensation. This conception is supported by the fact that where olfactory cells are present, as in some of the lower animals, their basal processes join the fibers of the olfactory nerve.

PARANASAL SINUSES. The bones surrounding the nasal cavities contain a number of spaces, the *accessory nasal sinuses.* They are known, according to the bones in which they are located, as the *maxillary, frontal, sphenoid* and *ethmoid sinuses.* These spaces, which are filled with air, communicate with the nasal fossae. The mucous membrane which forms their lining is similar to that which forms the lining of the fossae, except that it is considerably thinner. It consists of a pseudostratified epithelium, a thin basement membrane and an areolar stroma which blends with the periosteum, and in which a number of scattered lymphocytes are present. A few small mucous glands occur in the maxillary sinus.

THE LARYNX

The larynx is a large irregularly shaped, tubular chamber located between the pharynx and the trachea. It consists of a framework of cartilage bound together by elastic membranes and muscles. It is lined by a mucous membrane which is continuous above with that lining the pharynx and below with the mucous membrane lining the trachea. The principal cartilages of the larynx are the *thyroid*, the *cricoid*, and in addition, the small *arytenoid*, *corniculate*, and *cuneiform cartilages* which are associated with the organs of speech.

The thyroid and cricoid cartilages consist of hyaline cartilage, while the cuneiform, the corniculate, and the vocal processes and tips of the arytenoid cartilages are of the elastic variety. The *epiglottis* is a broad, flaplike structure, located above the opening *(aditus)* into the larynx. This opening is closed when the larynx is drawn up and pressed tightly against the epiglottis. The epiglottis is a membranous structure supported by a flattened plate of elastic cartilage. Small nodules of fibrous cartilage are frequently, but not constantly, found in the ligaments associated with the larynx.

The lateral walls of the larynx are provided with two horizontal folds, a pair on each side of their inner surface. These are the superior folds *(plicae ventriculares)* or *false vocal cords*, and the inferior folds *(plicae vocales)* or *true vocal cords.* The expanded portion of the larynx above the superior folds is called the *vestibule.* Between the superior folds and the inferior folds are two lateral expansions or diverticula called the *laryngeal ventricles.* Sometimes these laryngeal ventricles may extend as narrow pouchlike prolongations to the upper borders of the thyroid cartilages and form what are known as the *ventricular recesses.* The interval between the true vocal cords is quite narrow, but may be altered by the action of the *arytenoid* and *vocalis muscles.* Below the level of the true vocal cords the larynx is somewhat compressed, but within a very short distance increases in diameter and is continuous with the trachea at the level of the cricoid cartilage.

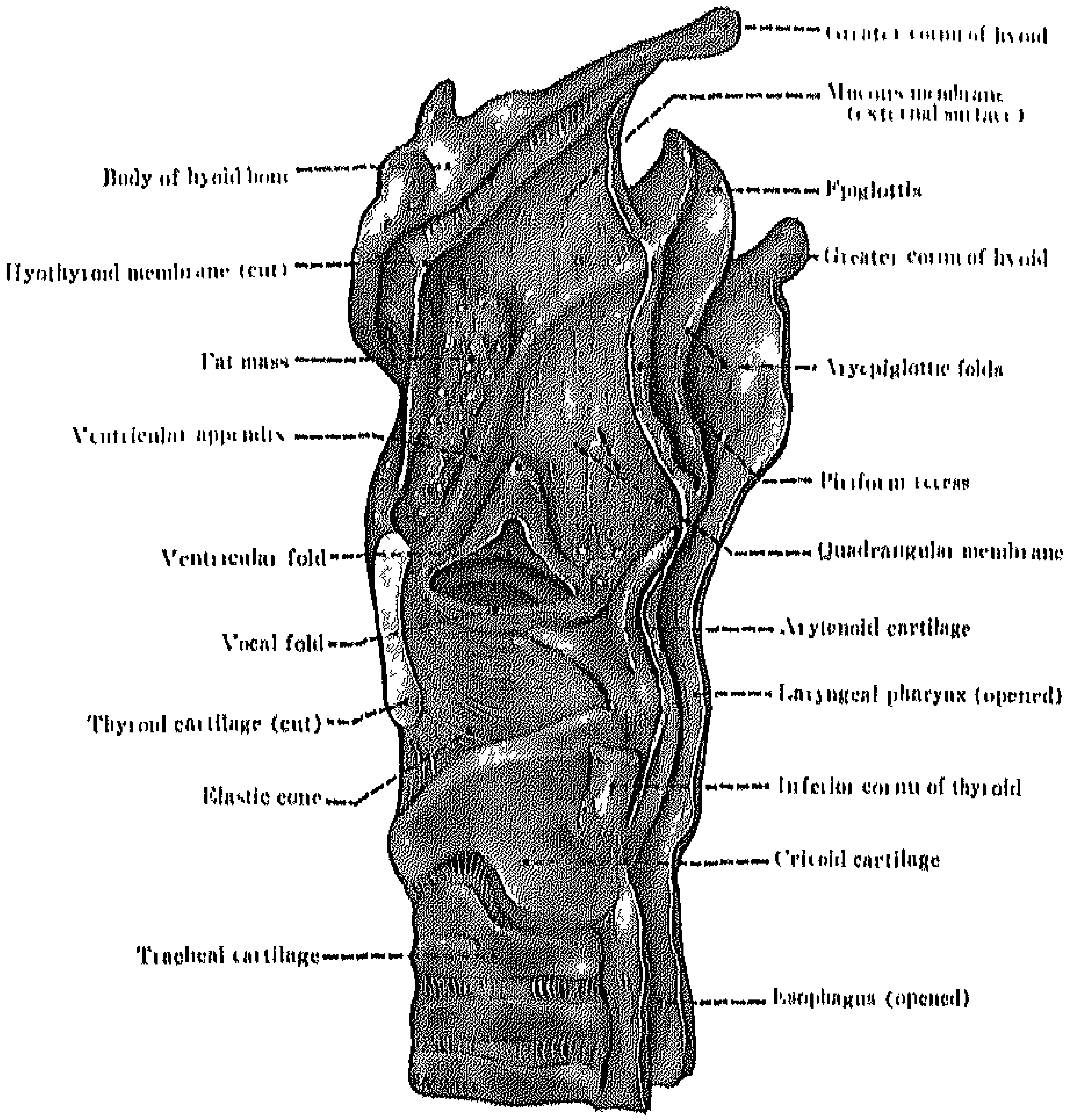


FIG. 171. The larynx and certain related structures viewed from the left. The left lamina of the thyroid cartilage has been removed and the laryngeal ventricle opened. All muscles have been removed and the hyothyroid membrane partially cut away. (Courtesy, J. Parsons Schaeffer, Ed.: "Morris' Human Anatomy," Philadelphia, The Blakiston Company.)

The pharyngeal surface of the epiglottis is covered by a mucous membrane which consists of a stratified squamous epithelium resting on a thin stroma of areolar connective tissue. As this membrane extends over the border of the epiglottis to its laryngeal surface, the epithelium changes to the respiratory (pseudostratified) type. The pseudostratified epithelium is continued downward over the superior folds and forms the lining of the laryngeal ventricles. It is interrupted by a narrow stretch of stratified squamous epithelium as it passes over the borders of the true vocal cords, after which the pseudostratified type of epithelium again continues to form the lining of the remainder of the larynx and also of the trachea.

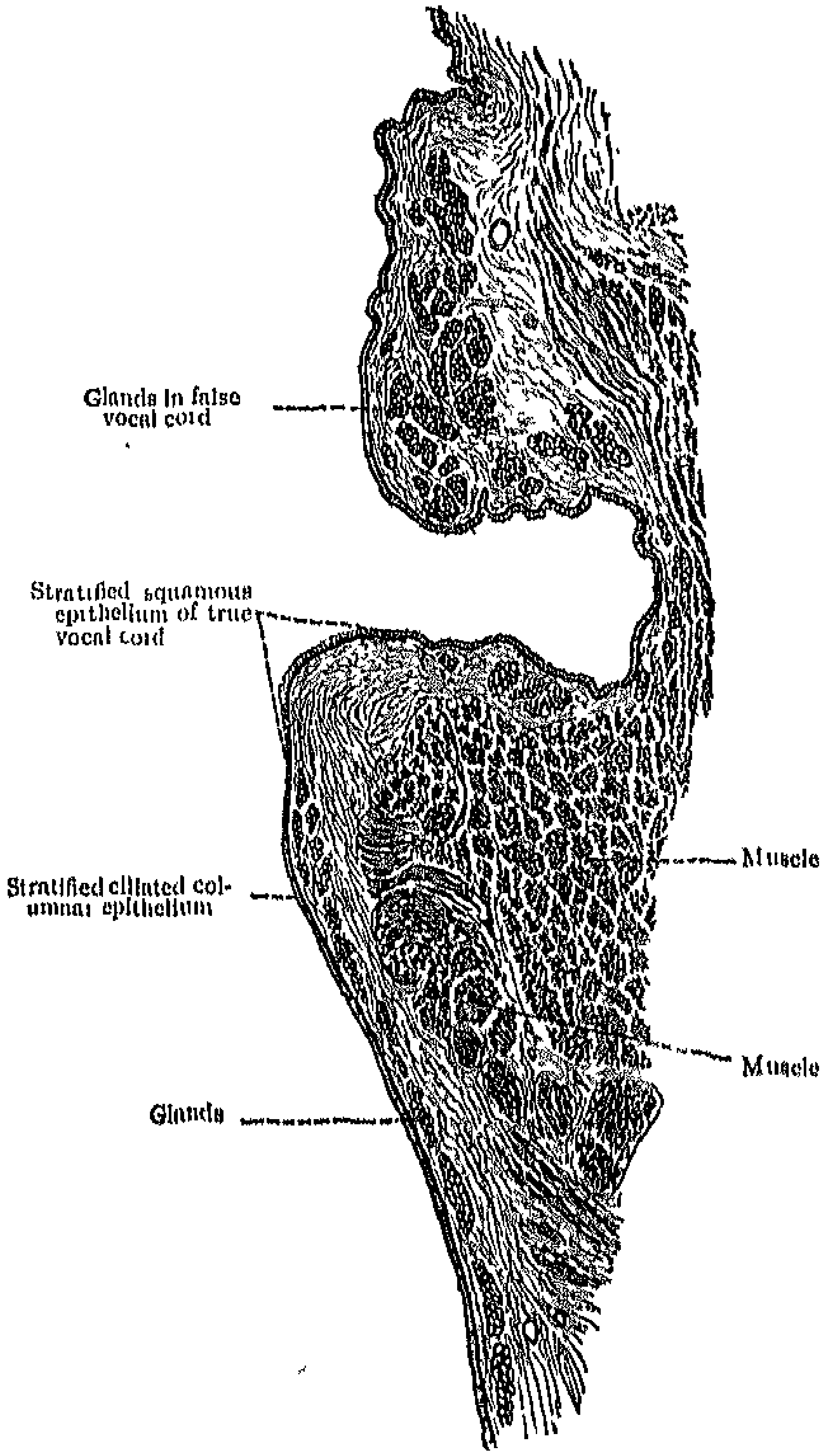

Glands in false vocal cord
Stratified squamous epithelium of true vocal cord
Stratified ciliated columnar epithelium
Glands
Muscle
Muscle

FIG. 172. Longitudinal section through the superior and inferior laryngeal folds (false and true vocal cords). (Courtesy, Böhm, Davidoff, and Huber: "Text-book of Histology," Philadelphia, W. B. Saunders Co.)

The columnar cells of the laryngeal epithelium are ciliated, the movement of the cilia being toward the outlet of the larynx. The deep surface of the stratified squamous epithelium, wherever it occurs in the larynx, is penetrated by papillae from the underlying connective tissue. The papillae are arranged so that they form parallel ridges where the epithelium passes over the vocal cords.

There is considerable variation in the epithelium lining the larynx.

It may consist, throughout, of an unmodified pseudostratified epithelium with the exception of that which passes over the vocal cords, or it may consist of areas of pseudostratified epithelium alternating with areas of stratified squamous epithelium, or it may be a stratified squamous epithelium with none of the pseudostratified form appearing except in the larger ducts of the glands associated with the larynx. However, this latter condition is rare. The change from the pseudostratified columnar to the stratified squamous type of epithelium is probably induced by a prolonged irritation of the membrane or excess aeration of the membrane.

The term, pseudostratified, is usually applied to the epithelium which lines the upper part of the respiratory passages. However, the depth of the epithelium in the larynx and trachea, and the number of cell layers which may be observed in the majority of cases, make it difficult to believe that this is not a true stratified columnar epithelium.

Except where it passes over the vocal cords, the epithelium of the larynx rests on a *tunica propria*, which consists of delicate connective tissue fibers with a rich intermingling of elastic tissue. Numerous lymphocytes are present in the region of the superior folds and in the tissue around the laryngeal ventricles. This lymphoid tissue often appears in the form of nodules.

External to the tunica propria is a layer of coarser collagenous fibers with an intermingling of elastic fibers, forming the *submucosa*. This layer is quite thin on the laryngeal surface of the epiglottis and over the vocal cords. It attains its greatest thickness in the superior folds and about the laryngeal ventricles where it contains groups of mixed serous and mucous glands of the tubuloacinar type. These glands are numerous in the region of the false cords and absent or only occasionally found in the true vocal cords. It also contains a number of large, thin-walled blood vessels which are readily distended, giving the submucosa the appearance of erectile tissue. When these vessels are filled with blood, the temperature of the folds is raised and the inspired air becomes warmer as it passes over them.

The true vocal cords are formed by a modification of the mucous membrane which passes over the free borders of the cricothyroid membrane. The elastic fibers in the border of this membrane are attached to the thyroid cartilage in front and to the vocal processes of the arytenoid cartilages behind, forming the *thyroarytenoid ligaments*. The tension of these ligaments is effected by the action of the *thyroarytenoid muscles*. The stratified squamous epithelium which passes over the borders of the folds is separated from the ligaments by a thin layer of densely compacted collagenous and elastic fibers.

The blood supply of the larynx is through a number of large vessels which form a network in the submucosa. The branches arising from this network break up into capillaries which pass to the glands and epithelium.

Lymphatics are abundant in the submucosa, their principal vessels draining into the cervical lymph nodes.

The nerve fibers which pass to the larynx are both myelinated and unmyelinated. The myelinated fibers are both sensory and motor. The sensory fibers end in sensory corpuscles and in free fibers located between the cells of the epithelium. The motor fibers end in the laryngeal muscles. The unmyelinated fibers are from the autonomic system and end in the walls of the blood vessels and ducts.

THE TRACHEA

The trachea begins at the inferior border of the cricoid cartilage and extends downward, for a little more than four inches, to the upper part of the thorax where it divides into the right and left bronchi, the right bronchus going to the right lung and the left bronchus to the left lung. It consists of a framework of C-shaped cartilaginous plates which are joined together by a dense connective tissue layer. These cartilages are incomplete posteriorly, the space between their free ends being occupied by fibrous and muscular tissue. The tube thus formed is lined by a mucous membrane.

Glands are found in the trachea and are of the tubuloacinar type. The mucosa of the trachea consists of a pseudostratified columnar ciliated epithelium which rests on a well-defined basement membrane. Four types of cells can be identified in the epithelium. The *basal cells* form the deepest row and rest on the basement membrane. Their nuclei are round or oval, with the long axis of the nuclei parallel to the basement membrane. *Intermediate cells* form the second row. These cells are often spindle-shaped due to the pressure of surrounding cells. They may extend the full width of the epithelium. In *ciliated columnar cells*, the outer surface has a ciliated, cuticular border. These cells extend the width of the epithelium and the portion of the cell in contact with the basement membrane is narrower than the end toward the lumen. The number of *goblet cells* is less in the trachea than in the bronchi. Another cell, the lymphocyte, is found scattered throughout the epithelial layer.

It is thought that the basal cell gives rise to the intermediate cell, which in turn may differentiate into either ciliated columnar cells or goblet cells. Seldom are mitotic figures observed in the epithelium of either the trachea or bronchi.

As in the larynx, the epithelium may alternate between pseudostratified columnar and stratified squamous. When present, the stratified squamous is usually confined to the posterior part of the tracheal wall. In rare cases stratified squamous epithelium may form the entire

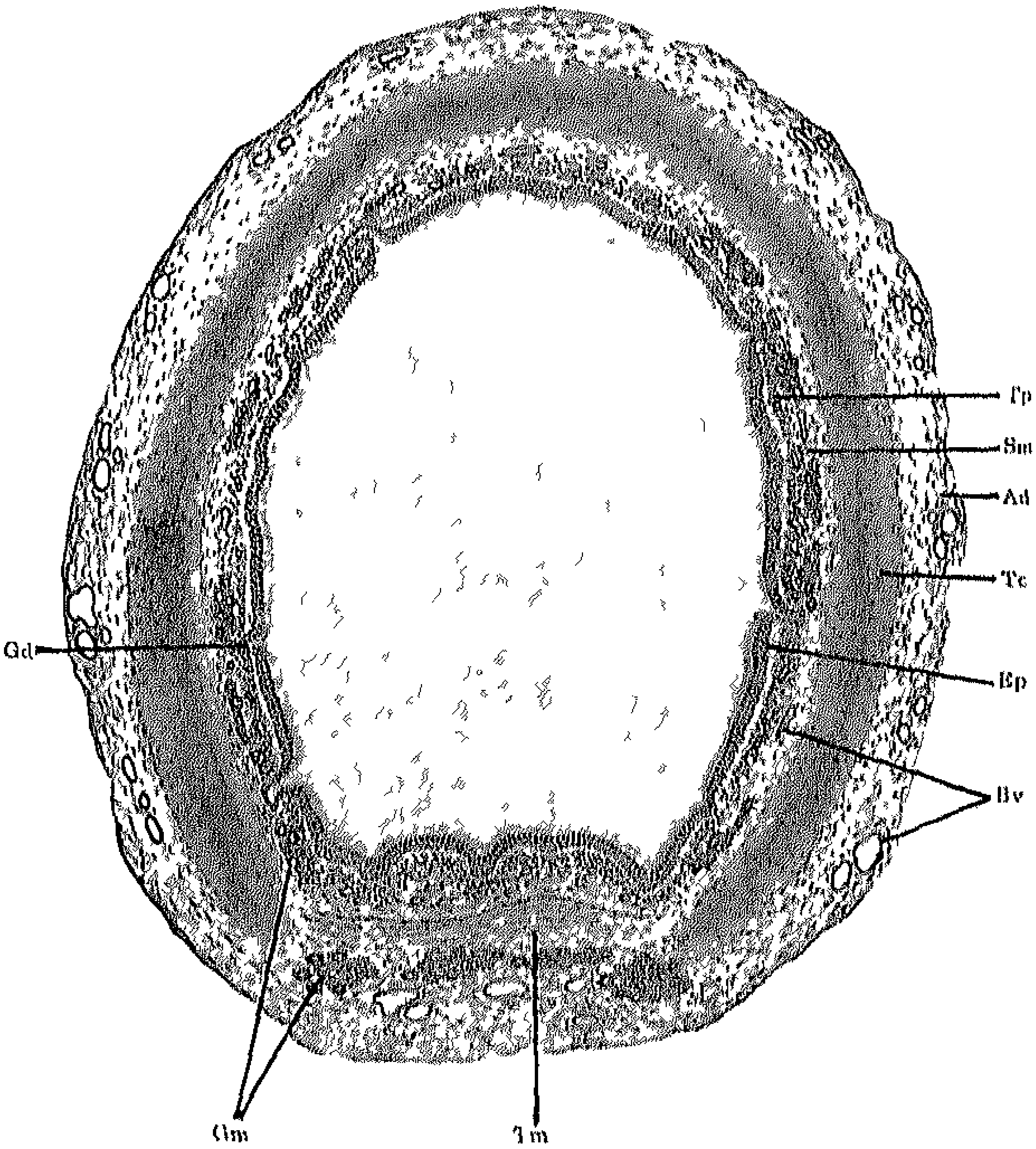


FIG. 178. Section through the trachea (human). (Ep) Stratified columnar epithelium. (Tp) Tunica propria. (Sm) Submucosa (Tc) Tracheal cartilage. (Ad) Adventitia. (Tm) Trachealis muscle. (Gm) Mucus-secreting glands. (Gd) Glandular duct. (Bv) Blood vessels

lining of the trachea as far as its bifurcation. When this occurs, pseudostratified epithelium is found in the lining of the large ducts.

External to the basement membrane is a layer of reticular tissue, the tunica propria. Numerous lymphocytes are scattered throughout this layer with, here and there, diffuse aggregations and small nodules of lymphoid tissue. The tunica propria is richly supplied with elastic fibers. Elastic fibers also form a layer between the tunica propria and the submucosa which is the equivalent of the muscularis mucosae in the wall of the alimentary canal.

The submucosa consists of loosely arranged collagenous and elastic fibers located between the mucosa and the tracheal cartilages. This tissue becomes condensed about the surfaces of the cartilages and joins the perichondrium. The submucosa gives support to blood vessels and lymphatics. In addition, it contains small groups of serous and mucous glands, some of which are so deeply placed that they lie in the tissue between the tracheal cartilages. The ducts which convey the secretions from these glands pass through the mucosa and open on the surface of the epithelium.

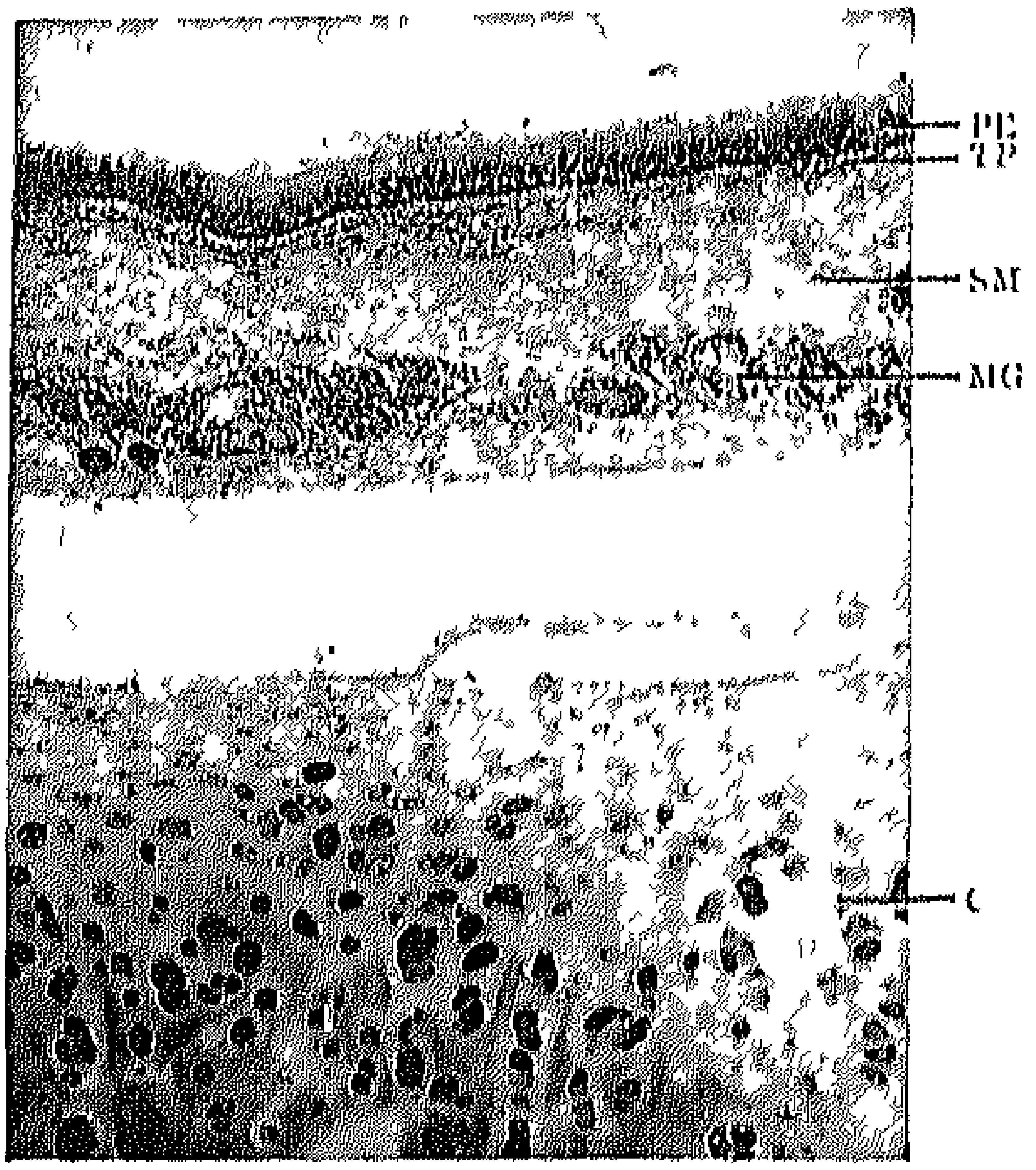


FIG. 174. Portion of the trachea. (C) Tracheal (hyaline) cartilage. (MG) Mucous glands (PE) Pseudostratified epithelium (stratified columnar). (SM) Submucosa. (TP) Tunica propria. The space between the cartilage and the submucosa is due to the shrinkage of the tissue in making the preparation. Photomicrograph

These glands are more numerous in the anterior portion of the tube than laterally and are located in the submucosal layer. They are also found in the posterior wall, but here they are in the submucosa and muscular layers. Moreover, some of them lie deep to the muscle layer. In a longitudinal section of the trachea the glands are seen to be grouped between the cartilage plates.

The posterior wall of the trachea lies between the free ends of the tracheal cartilages. Its structure is similar to that of the other membranous portions of the trachea, consisting of a mucous membrane and a submucosa. The cartilaginous plate which is deficient in this area is replaced by the trachealis muscle.

In man, the transversely directed bundles of smooth muscle are attached to the perichondrium of the inner side of the cartilage a short distance from the tip. Longitudinally directed bundles of smooth muscle are seldom seen in man. Between the muscle layer and the mucosa is a dense layer of longitudinally directed elastic fibers. Owing to the abundance of muscular and elastic tissue in this portion of the tracheal wall, the mucous membrane is raised into a number of longitudinal folds.

The tracheal cartilages are enclosed and joined by a fibroelastic membrane which blends with their perichondrial layer and extends from the lower border of one cartilage to the upper border of the adjacent cartilage.

THE LUNGS

The lungs are large, saclike structures, light pink in color and having a soft, pliable texture. They are located in the pleural cavities

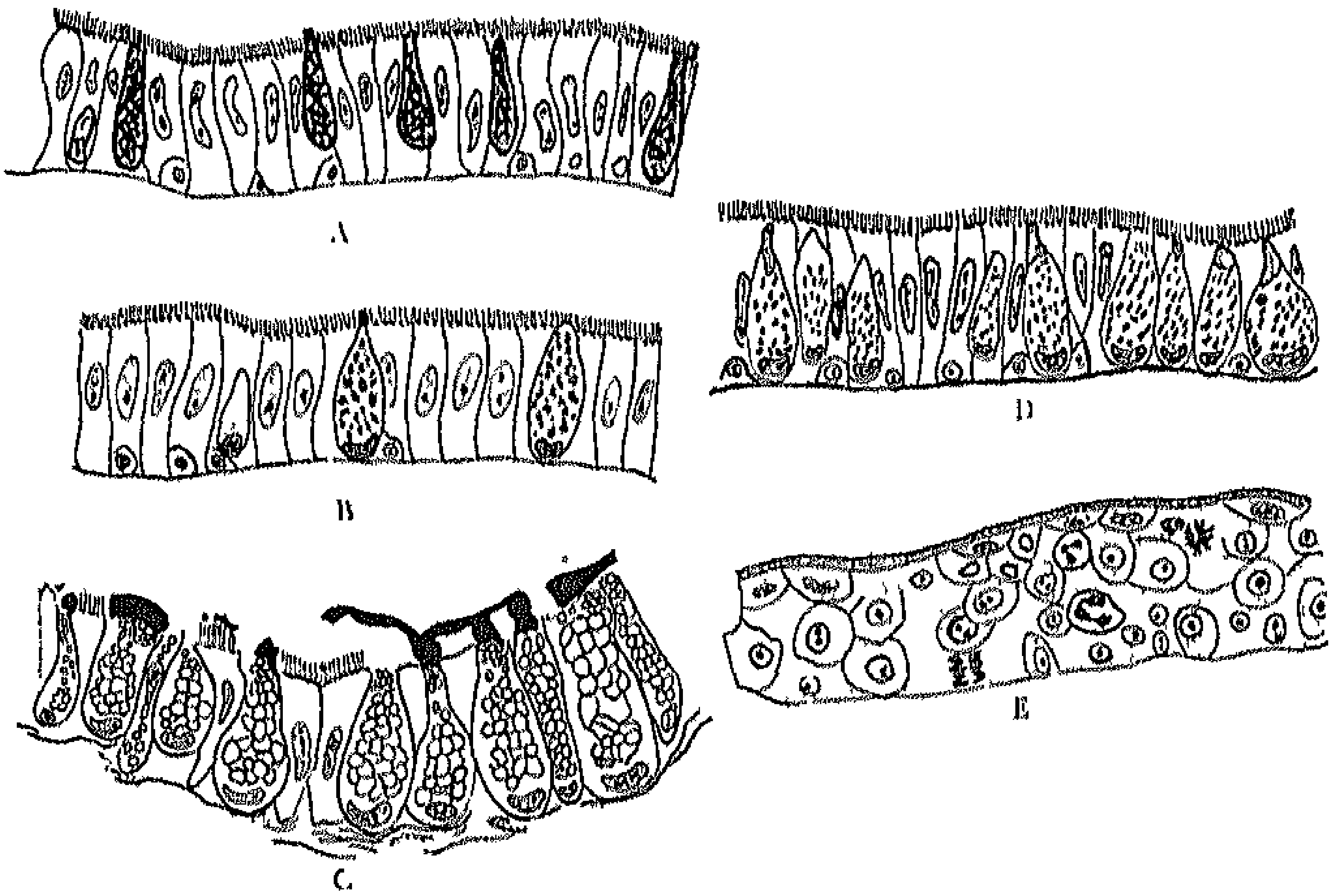


Fig. 175. Changes in tracheal epithelium. (A) Normal, showing mucus-containing goblet cells (cat). (B) After pilocarpine injection (cat). (C) Chronic bronchitis (human) showing marked increase in goblet cells. (D) After intratracheal injections of 0.125 per cent formalin (cat) to show resulting increase in size and number of goblet cells. (E) Stronger formalin causes a replacement of normal epithelium by protective stratified squamous epithelium. (Redrawn and modified from Flores, Carleton, and Wells: *Brit. J. Exper. Path.* Cowdry: "A Textbook of Histology," courtesy of Lea & Febiger.)

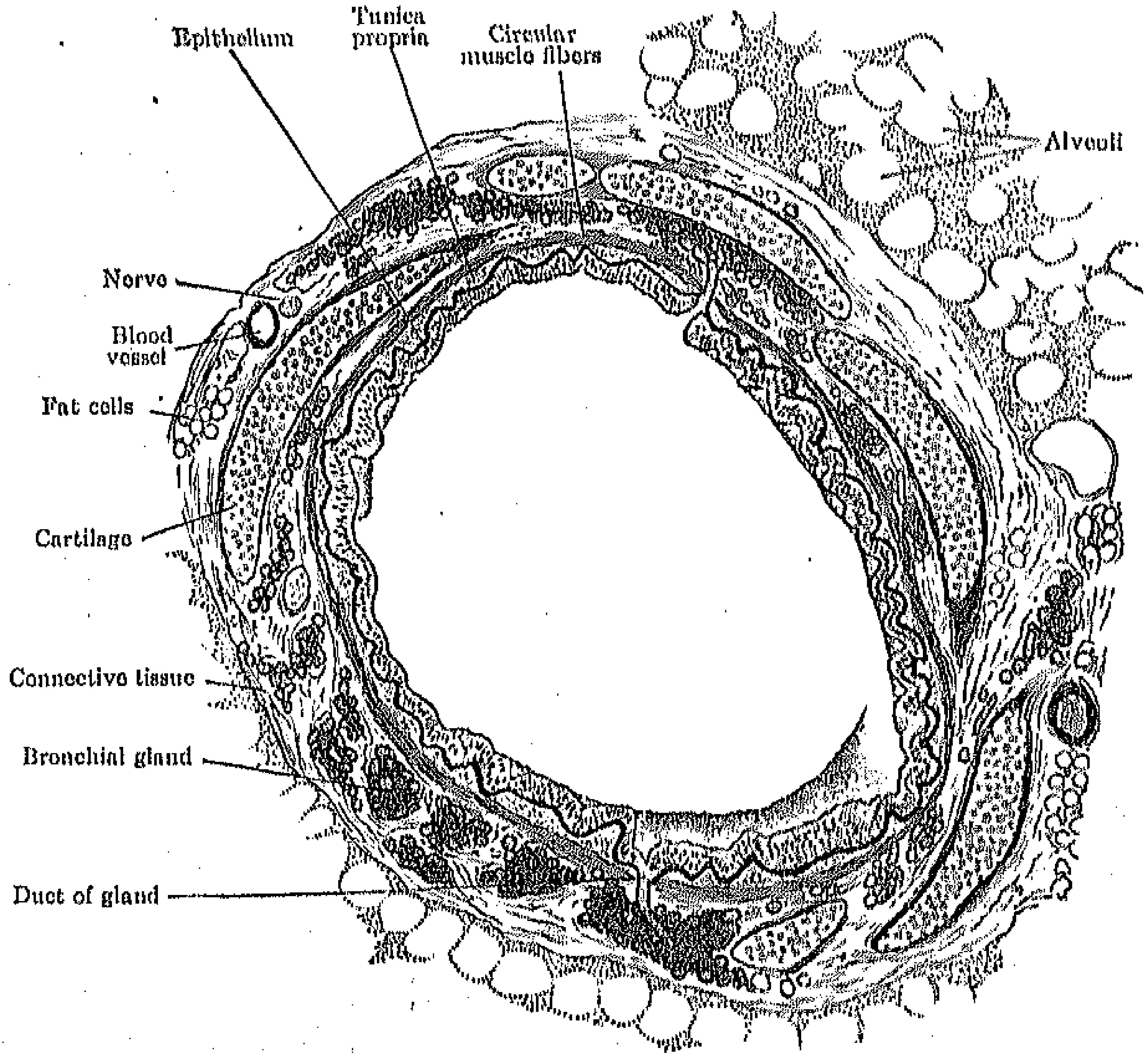
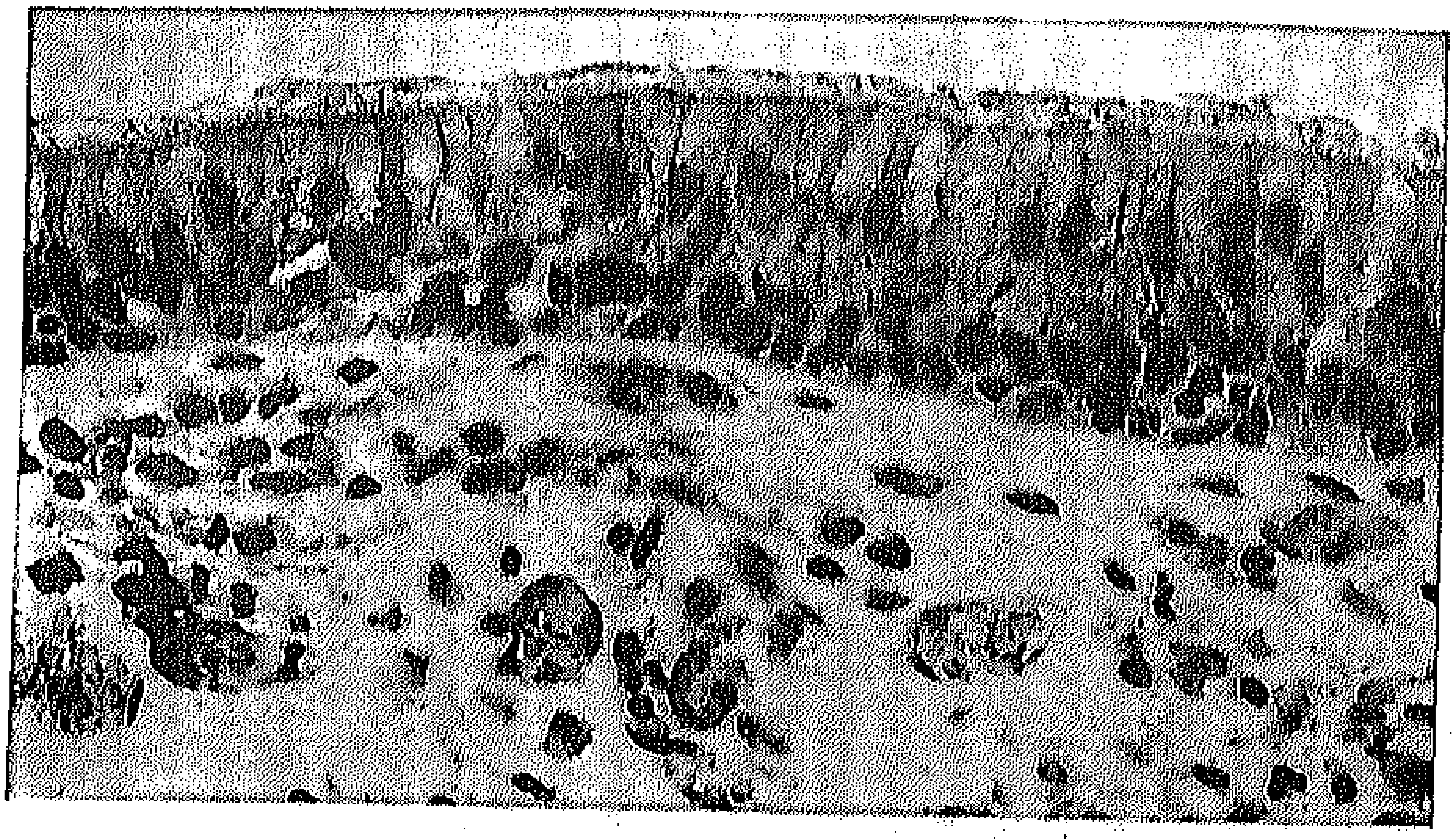


FIG. 176. Cross section of a bronchus 2 mm. in diameter, from a child. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

of the thorax. The trachea communicates with each lung by way of the right and left bronchi. Each lung is divided by deep fissures into lobes, the right lung having three lobes and the left lung two lobes. After entering the substance of the lungs, the bronchi divide into secondary branches which pass into the lobes. The bronchioles are formed by the repeated divisions of these branches, which decrease in size with each division, and finally end in the thin-walled air-spaces where the exchange of gases takes place between the inspired air and the blood. Owing to the treelike arrangement of the primary bronchus and its subdivisions, the entire system of tubules is often referred to as the *bronchial tree.*

With the repeated divisions of the bronchial tree, certain modifications take place in all of the layers of the walls of these tubular structures.

There seems to be much confusion concerning the exact points of division of segments of the bronchial tree and the point at which



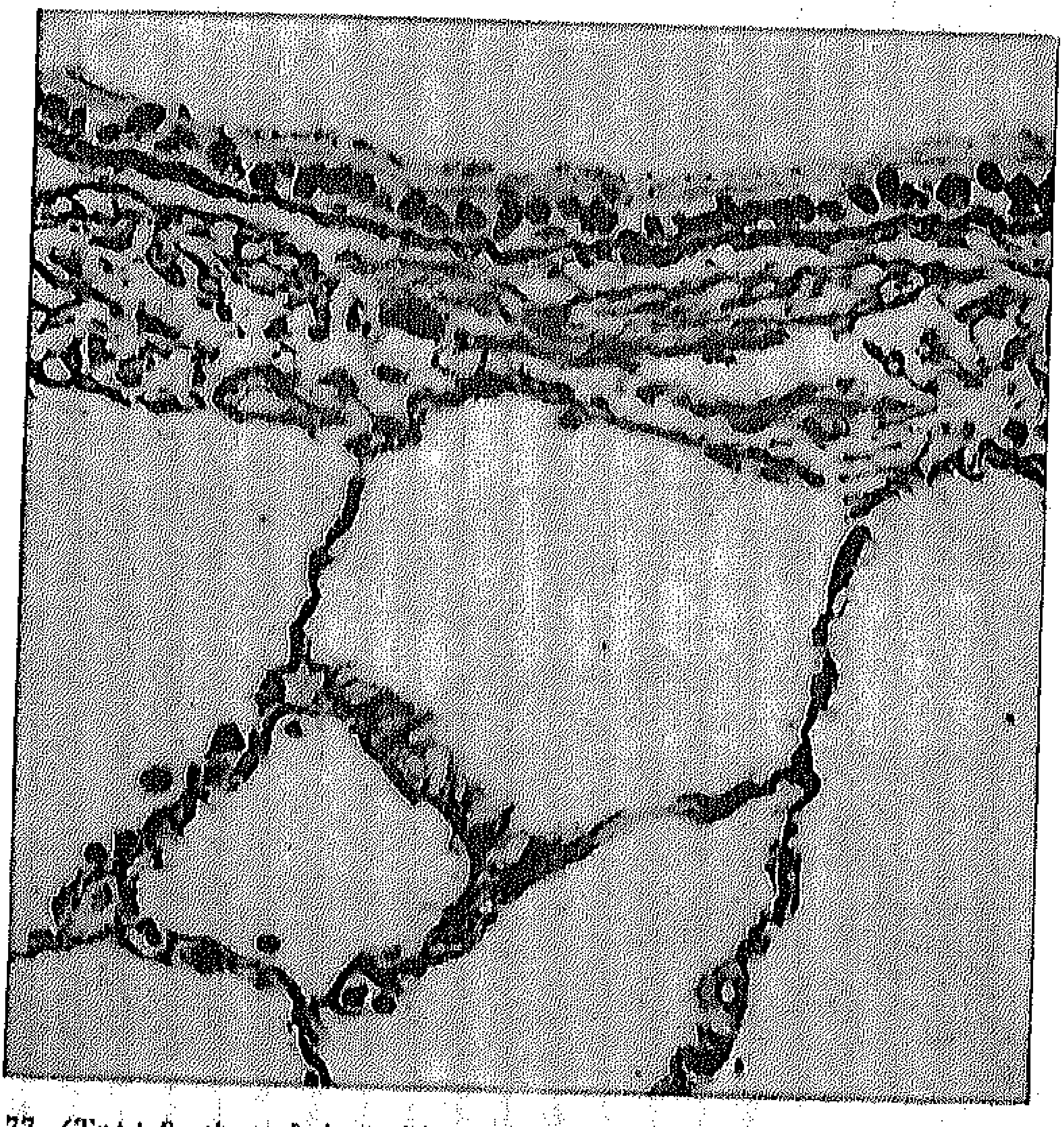


FIG. 177. *(Top)* Section of the epithelium lining bronchus 3 mm. in diameter. 500 ×. (From William Snow Miller: "The Lung," 2d ed. Courtesy of Charles C Thomas, Publisher, Springfield, Ill.)

FIG. 178. *(Bottom)* Section of a bronchiole 0.35 mm. in diameter. The epithelium has changed from a ciliated columnar to a ciliated cuboidal type. (From William Snow Miller: "The Lung," 2d ed. Courtesy of Charles C Thomas, Publisher, Springfield, Ill.)

certain definite changes occur in the walls of these structures. In the present discussion the classification will be based on the findings of W. S. Miller.

As the bronchi enter the substance of the lung they divide to form secondary bronchi. These in turn branch and the ultimate succession of divisions may be listed as follows: *secondary bronchi, bronchioles, terminal bronchioles, respiratory bronchioles, alveolar ducts, atria, alveolar sacs, alveoli.*

The epithelium gradually changes as it extends throughout the bronchial tree. From a pseudostratified columnar epithelium, the cells gradually assume a simple columnar arrangement and then the height of the cell decreases until it becomes cuboidal and finally squamous. Goblet cells decrease in number and finally disappear, and the ciliated cells lose their cilia.

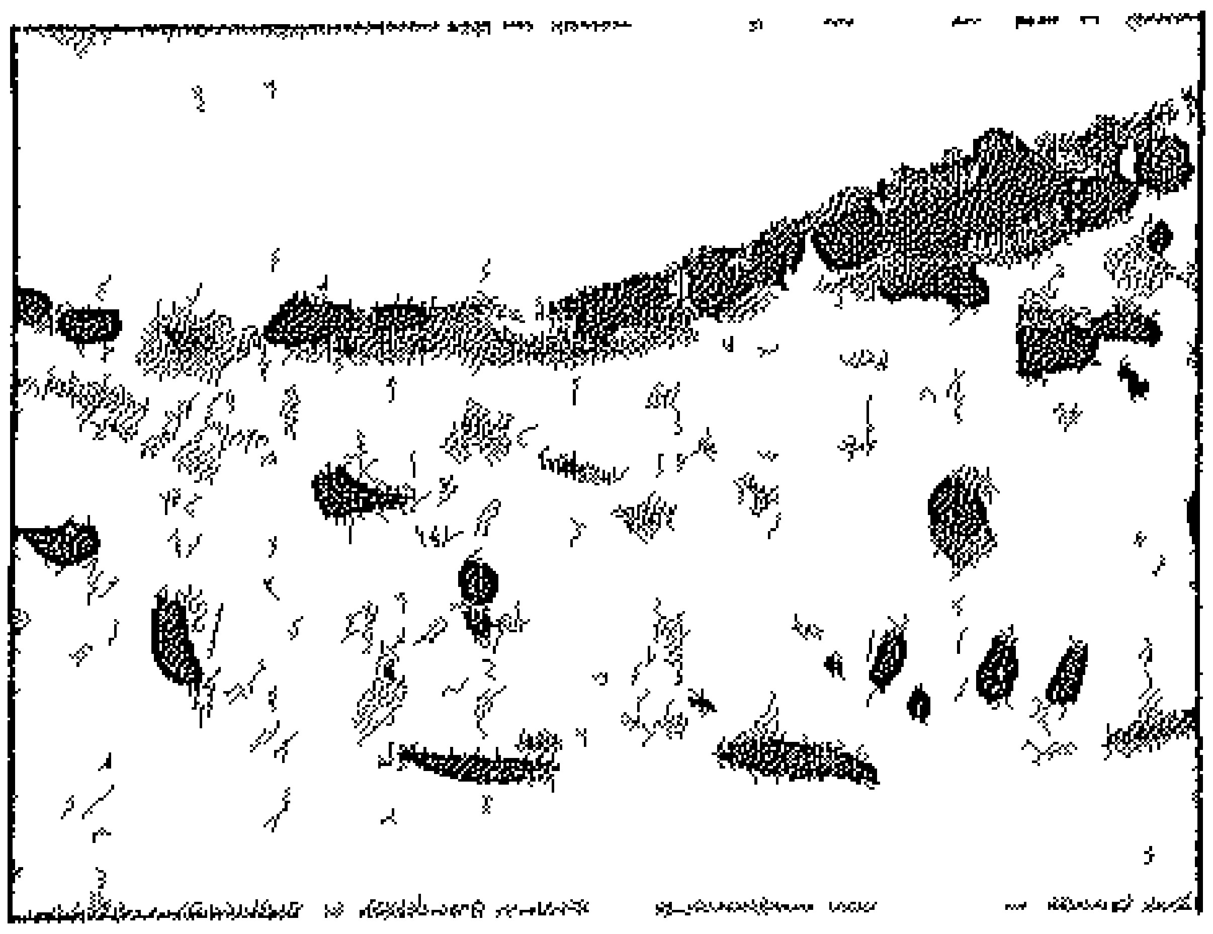


FIG. 179 Longitudinal section of a bronchiole 0.35 mm. in diameter On the right are a few ciliated cuboidal cells To the left they have given way to a nonciliated cuboidal epithelium. (From William Snow Miller: "The Lung," 2d ed Courtesy of Charles C Thomas, Publisher Springfield, Ill.)

In bronchioles having a diameter of 1 mm. the thickness of the epithelial layer decreases. There is an increase in the number of ciliated cells accompanied by a decrease in the number of goblet cells, which become quite scarce and finally disappear in bronchioles of 0.4 mm. (these are the terminal bronchioles). The basal cells are still present. The height of the epithelial cells gradually decreases and in bronchioles of 0.3–0.4 mm. the cells become cuboidal, still, however, retaining their cilia. The basal cells become extremely scarce and the basement membrane is reduced to a very thin layer. In the respiratory bronchiole, the ciliated cuboidal cell has disappeared and is replaced by a nonciliated cuboidal type of epithelium which extends throughout the respiratory bronchiole In the alveolar ducts this cuboidal epithelium gradually flattens to the squamous type of epithelium (respiratory epithelium) which lines the pulmonary alveoli.

The C-shaped cartilages of the trachea and bronchi are transformed into cartilaginous plates in bronchioles having a diameter of .96 mm. Several of these cartilaginous plates encircle the wall of the bronchioles. In bronchioles having diameters of 0.6–0.7 mm. (terminal bronchioles) the cartilage entirely disappears.

In the secondary bronchioles and their branches the circular layer of muscle has increased until it completely encircles the bronchiole inside the cartilage. Moreover, there is a relative increase in quantity of muscle (in relation to the diameter of the tube) from the bronchioles to the alveolar ducts. At the distal end of the alveolar ducts the circular muscle layer forms a sphincter muscle and terminates.

From the above discussion it can be seen that the greatest changes occur prior to the terminal bronchioles. These bronchioles are lined by cuboidal, ciliated epithelium but contain no goblet cells, no glands and no cartilage. At the distal end of the terminal bronchioles the purely conducting system of ducts also terminates.

Beginning with the respiratory ducts, alveoli are present along the walls of these ducts, the atria and the alveolar sacs; and these structures assume a respiratory function. Each respiratory bronchiole, which is both conducting and respiratory in function, terminates in an alveolar duct, which is the first segment of the primary lobule (structural unit) of the lung. A primary lobule may thus be defined as consisting of the alveolar duct, atria, alveolar sacs and alveoli, along with the vessels and nerves which accompany them.

Attention should be called to the fact that there are two types of alveoli present in the lungs: those which open into the respiratory bronchioles and alveolar ducts, both of which structures have muscular fibers in their walls, and those that open into the atria and alveolar sacs, whose walls are devoid of muscle fibers. Over-distention of the alveoli of the first type is prevented by the sphincter action of the muscles guarding their entrance. In the second type where no muscles are present the alveoli are covered by a network of elastic fibers which prevent overdistention. These elastic fibers are circularly arranged at the junctions between the alveolar ducts and atrium; atrium and alveolar sacs; and alveolar sacs and alveoli.

The respiratory bronchioles may branch one or two times before they terminate in the several alveolar ducts. Each alveolar duct, in turn, opens into several more or less spherical spaces called atria, which communicate with several irregularly shaped chambers, the alveolar sacs. Opening all along the walls of the alveolar sacs and atria are small spaces known as alveoli. Alveoli also open into the alveolar ducts, and a few into the respiratory bronchioles, from the presence of which these bronchioles derive their name.

The lack of uniformity in describing the subdivisions of the pulmonary structures is probably due to differences in the complexity of their arrangement. Thus, the alveolar ducts may be connected with a terminal bronchiole by a single respiratory bronchiole. On the other hand, two or more orders of respiratory bronchioles may intervene between the terminal bronchioles and the alveolar ducts. Consequently, almost any description of these subdivisions must lack precision. In general, however, the foregoing description presents the main features of the subdivisions of the pulmonary structures.

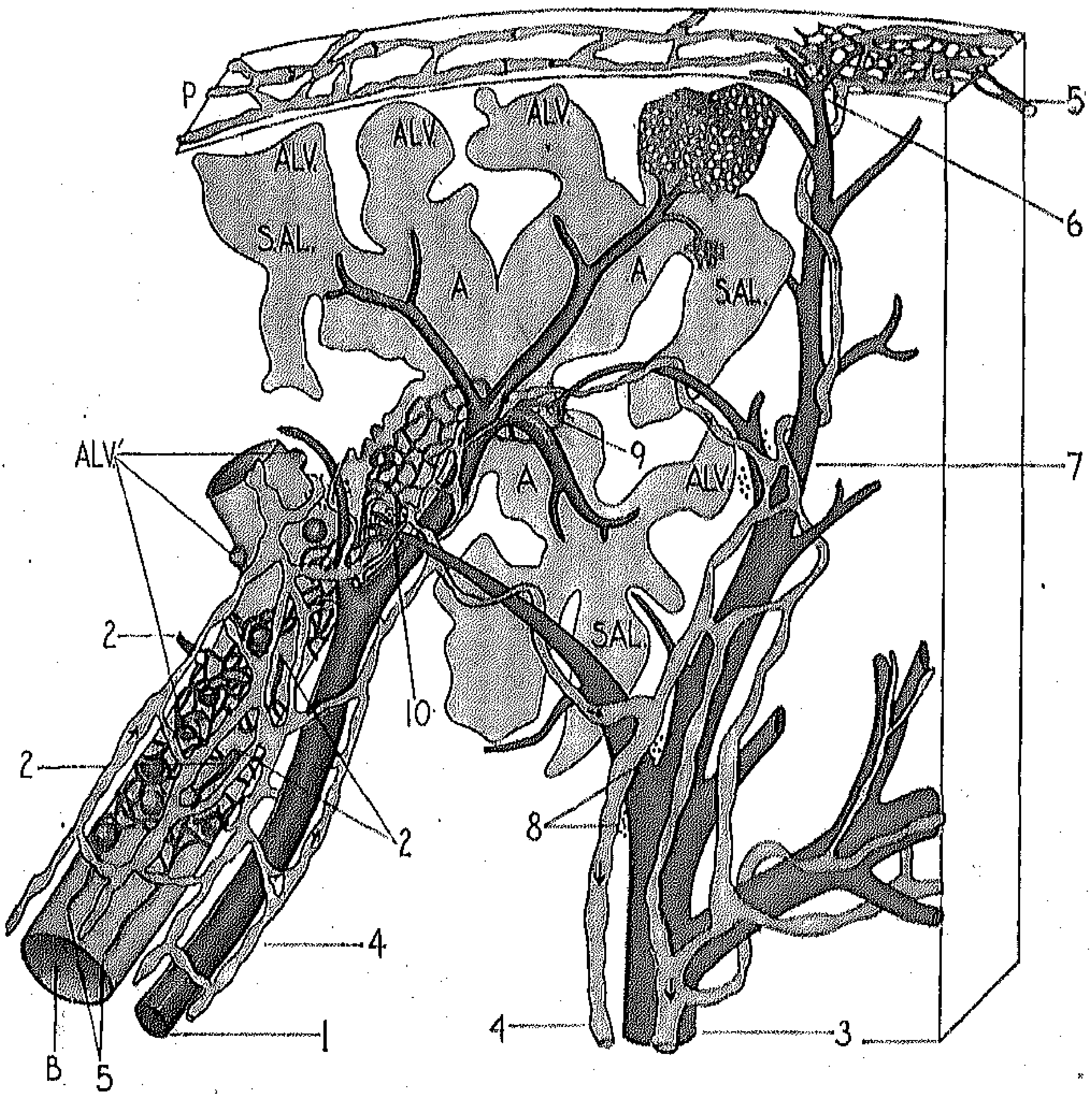


FIG. 180. Diagrammatic representation of a primary lobule showing the subdivisions of the bronchial tree, the pulmonary artery and vein, the lymphatics, and the lymphoid tissue. (A) Atria. (B) Respiratory bronchiole. (ALV.) Pulmonary alveoli. (ALV.') Alveoli scattered along the respiratory bronchiolus and alveolar ducts. (S.AL.) Alveolar sacs. (P) Pulmonary pleura. (1) Pulmonary artery with its branches. (2) Branches of pulmonary artery which are distributed to the respiratory bronchioles and alveolar ducts and then form capillaries which join capillaries from the bronchial artery. (3) Pulmonary vein with its tributaries indicated at 6, 9, 10, and from the capillary network at the distal end of a radicle of the pulmonary artery. (4) Lymphatics (arrows indicate direction of lymph flow). (5) Bronchial artery and terminal capillary network which unites with capillaries derived from the pulmonary artery. (5') Bronchial artery contributing to the formation of the capillary network within the pleura. (6) A radicle of pleural vein arising from the capillaries in the pleura, derived from the bronchial artery. (7, 8, 9, 10) Where lymphoid tissue is found. (From William Snow Miller: "The Lung," 2d ed. Courtesy of Charles C Thomas, Publisher, Springfield, Ill.)

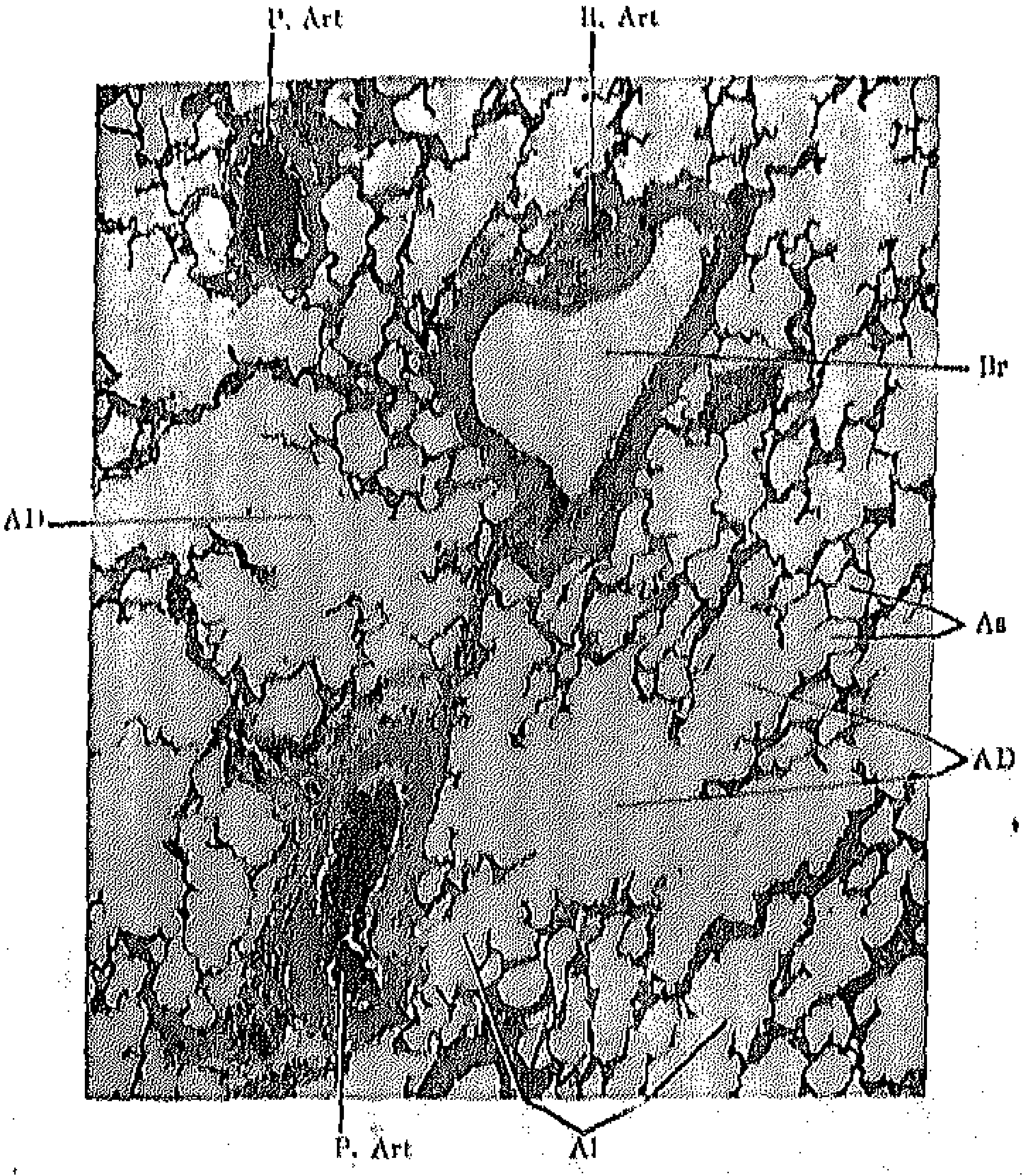


FIG. 181. Pulmonary tissue. (AD) Alveolar ducts. (Al) Alveoli. (As) Air (alveolar) sacs. (B. Art.) Bronchial artery. (Br) Bronchiole. (P. Art) Pulmonary artery. Photomicrograph.

PULMONARY ALVEOLI

The walls of the pulmonary alveoli are dominated by the capillaries which form dense plexuses around them. Supporting these capillaries and representing the remaining constituents of the walls are fine elastic fibers and a few collagenous fibers. Reticular fibers are also present and form a very fine delicate membrane just beneath the epithelium. This form of structure allows for the expansion and contraction of the alveoli during the act of breathing. In the connective tissue of the walls of the alveoli there are a few connective tissue cells, especially certain types of wandering cells (macrophages) which are known as *septal cells.*

There is considerable difference of opinion concerning the morphology of the structural elements lining the pulmonary alveoli. One group denies the existence of any epithelial layer lining the air cells. In this case the underlying connective tissue elements alone are thought to separate the capillaries from the alveolar air. On the other hand, a second group supports the idea that the pulmonary alveoli are lined

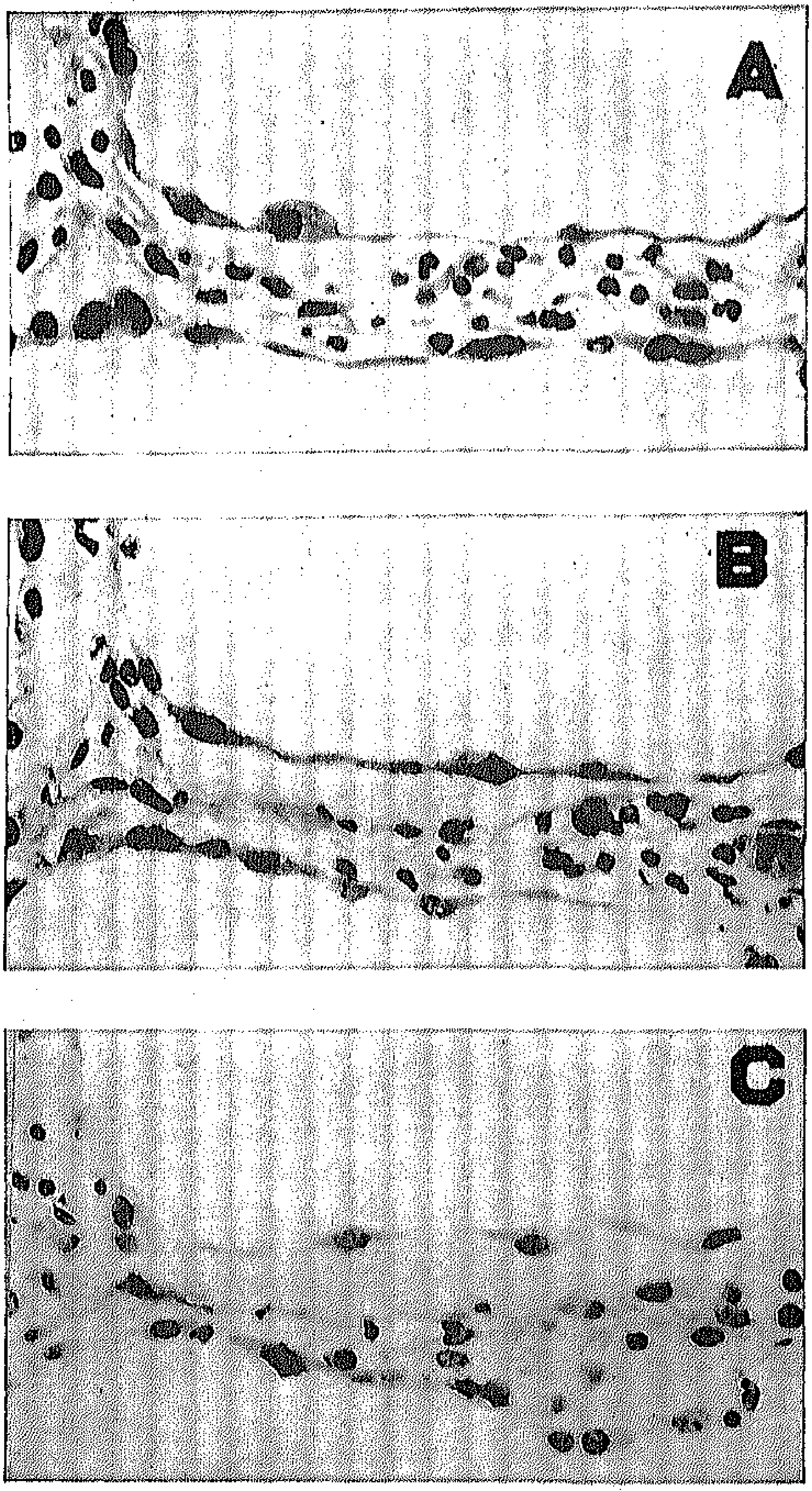


FIG. 182. Three sections from a series which show on their upper side the epithelium slightly raised from the surface of the alveolar wall by the exudate behind it. 500 X. (From William Snow Miller: "The Lung," 2d ed. Courtesy of Charles C Thomas, Publisher, Springfield, Ill.)

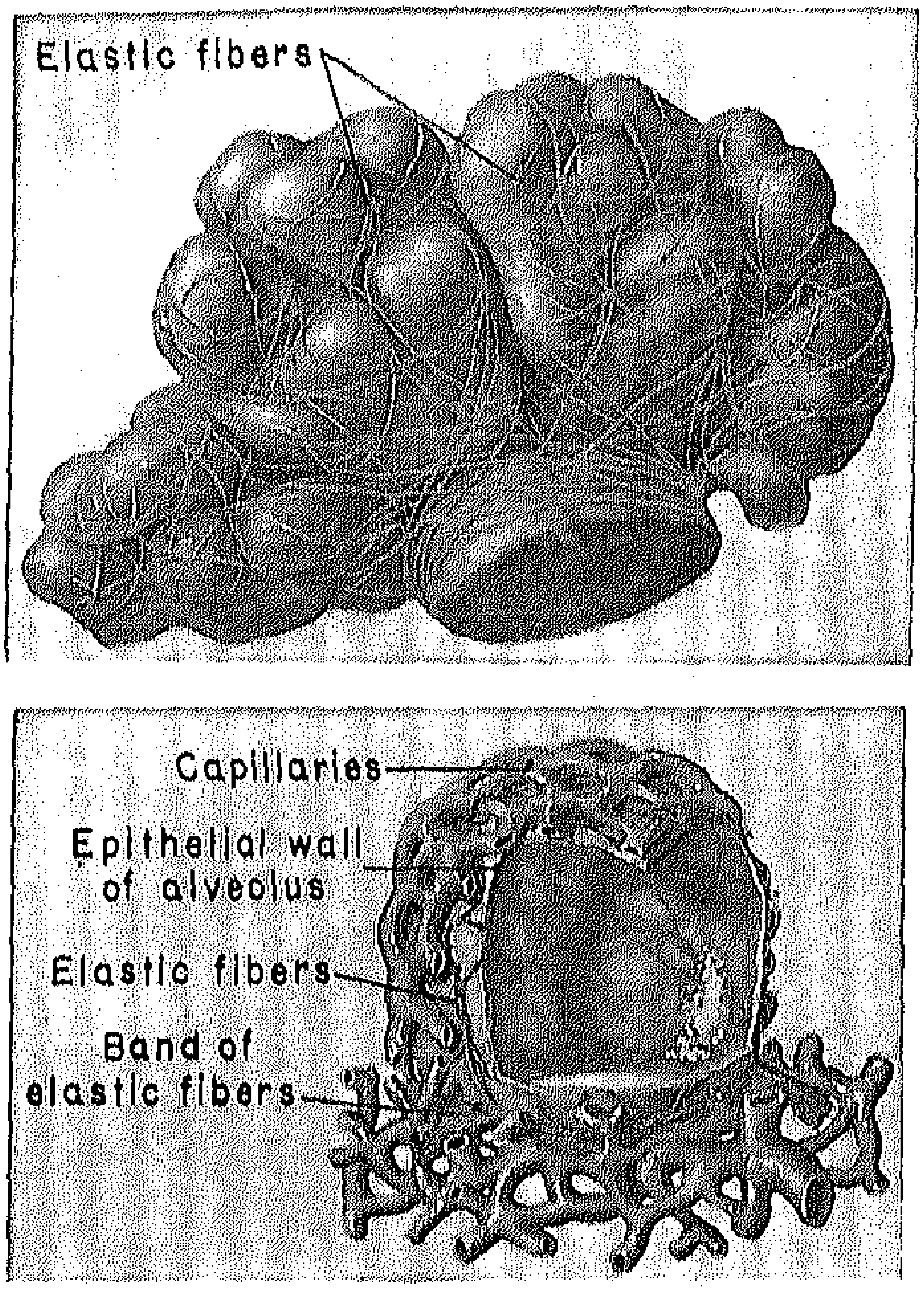


FIG. 183. *(Top)* Alveolar sac cut off from its atrium and showing the arrangement of the elastic fibers. Note the encircling band of elastic fibers at its junction with the atrium and the network of fibers which enclose the sacculus. *Semidiagrammatic.* *(Bottom)* Network of elastic fibers surrounding and enclosing an alveolus.

by an epithelium, but disagree among themselves as to the exact nature of these epithelial elements. Some advance the idea that these air-spaces are lined by a peculiar type of epithelial element, namely, flattened, non-nucleated protoplasmic plates among which are scattered smaller, thicker cells containing nuclei. It is thought that when some of the epithelial plates are lost, they are replaced by the thicker cells flattening out and losing their nuclei. The other group believes that the alveoli are lined by an epithelial layer in which all the cells are nucleated. W. S. Miller represents this group and he has presented conclusive evidence, based partly on the study of edematous alveolar tissue, that there is present in the alveoli a distinct epithelial layer in which the cells are nucleated. He describes this layer as being made up of "thin, flattened, nucleated squames" which form a continuous epithelial lining.

Large cells resembling macrophages are often found lying in the alveoli. They are believed to be derived from the septal cells of the alveolar wall. On account of their being filled with particles of dust they are known as *dust cells*. It has been suggested that, after collecting the particles of dust which have been deposited in the alveoli, these cells convey them to the lymph nodes in the hilum of the lung, in which they are finally stored. Similar cells have been found in certain conditions of heart disease to be filled with hemosiderin, and are known as *heart failure cells*. When the pulmonary tissues of persons working in a heavily dust laden atmosphere become filled with particles of dust, the condition is known as *anthracosis*.

THE PLEURA

The pleura is a two layered serous membrane. The visceral layer is tightly adherent to the entire surface of each lung and at the root of the lung is reflected onto the walls of the pleural cavity as the parietal layer. The pleura consists of a lining of flattened mesothelial cells supported by a thin stroma of delicate connective tissue in which may be found a few scattered bundles of smooth muscle. This tissue is continuous with the connective tissue between the lobules of the lungs and contains blood vessels, lymphatics and nerves.

BLOOD SUPPLY. The blood supply of the lungs is received from two sources, both of which gain entrance by way of the lung root. The *pulmonary arteries* carry venous blood that is to have its oxygen supply renewed, and the *bronchial arteries* which convey arterial blood carry nutritive materials and oxygen from the systemic circulation to the lung tissues. The pulmonary and bronchial veins return the blood to the heart.

On entering the root of the lung, the pulmonary vessels branch repeatedly with the branching of the bronchial tree and follow these structures into the primary lobule. At the beginning of the alveolar ducts these small vessels break up into the capillary networks which are found in the alveolar walls. These capillaries unite to form the pulmonary veins which lie, at first, close to the surfaces of the lobules, their branches entering the interlobular connective tissue, in which they unite to form the larger veins. These veins follow the course of the pulmonary arteries and interlobular bronchioles and finally emerge at the hilum as the pulmonary veins.

The bronchial arteries arise directly from the aorta or some of its branches. They accompany the divisions of the bronchioles as far as the terminal portions of the respiratory bronchioles. These vessels and their branches are located in the walls of the bronchi and bronchioles, the tissues of which they supply. The terminal bronchial capillaries which are formed in the region of the respiratory bronchioles do not extend into the primary lobule, but anastomose with the pulmonary

STRUCTURAL CHARACTERISTICS OF THE TRACHEA AND THE BRONCHIAL TREE

		Segment	Epithelium	Cartilage	Glands	Muscular Layer
Conducting portion		Trachea	Pseudostratified columnar, ciliated (Stratified squamous under certain conditions)	Present C-shaped	Branched tubuloacinar Mucous and serous	Smooth muscle between ends of C-shaped cartilage
		Bronchi	Pseudostratified columnar, ciliated More goblet cells than in trachea	Present C-shaped	Branched tubular	In primary bronchi it is the same as the trachea In secondary bronchi a complete circular layer develops
		Bronchioles	Thinner layer of pseudostratified columnar, ciliated Becomes simple columnar, ciliated Ciliated cells increased Goblet cells becoming scarce	Present in form of several cartilage plates	None	There is a relative increase in quantity of muscle from the bronchioles to the junction between the respiratory bronchioles and the alveolar ducts
		Terminal bronchioles	Cuboidal Ciliated cells present No goblet cells	None	None	
Respiratory portion		Respiratory bronchioles	Cuboidal No ciliated cells	None	None	
	Primary lobule	Alveolar ducts	Flattened cuboidal becoming squamous	None	None	Thin layer only Sphincter muscle at distal end of alveolar ducts
		Atria	Squamous	None	None	
		Alveolar sacs	Squamous	None	None	None, replaced by a network of elastic fibers
		Alveoli	Squamous	None	None	

capillaries which continue throughout the primary lobule. Thus a part of the blood brought into the lung by way of the bronchial artery is returned by way of the pulmonary veins, the remainder is returned through the bronchial veins.

LYMPHATIC SUPPLY. The lymphatic vessels of the lungs are arranged in two sets: superficial and deep. The superficial lymphatics begin as a capillary network which is located in the pleura. They receive afferent vessels from the deep lymphatics which are found throughout the lung substance. The deep lymphatics begin as capillaries about the pulmonary alveoli. These capillaries unite to form larger vessels which follow the course of the bronchial tree. Near the hilum of the lung, the vessels of the superficial plexus (draining the pleura) and the deep lymphatics (draining the substance of the lung) anastomose.

NERVE SUPPLY. The nerve supply is by both sympathetic and vagal parasympathetic fibers. Ganglion cells of the sympathetic are located in the cervical and upper three thoracic ganglia. From these ganglia, fibers pass to the musculature of the walls of the blood vessels and air passages. Stimulation of the sympathetic fibers produces bronchodilatation. The parasympathetic ganglion cells are found in the tracheal and pulmonary ganglia. From these ganglia, fibers pass to the trachea and bronchial tree where they end in relation to the musculature of these structures. Stimulation of the parasympathetic fibers causes bronchoconstriction. Myelinated fibers, which are probably sensory, end as fine naked fibrils in the tunica propria and between the epithelial cells of the bronchioles. These vagal afferents are important in regulation of rate and depth of respiration. The question of whether nerve fibers are present in the alveoli is still unsettled. So far at least they have not been satisfactorily demonstrated.

17

The Urinary System

The urinary system includes the structures which are concerned with the excretion of the urine and its elimination from the body. They are: the *kidneys*, the *ureters*, the *bladder*, and the *urethra*.

THE KIDNEYS

The kidneys are paired compound tubular glands located one on either side of the vertebral column in the back part of the upper abdominal cavity, behind the peritoneum. Each kidney is a flattened, bean-shaped structure about 4.5 inches (11.5 cm.) in length, 2–2.5 inches (5.5 cm.) in breadth, and about 1.5 inches (3.7 cm.) in thickness. The lateral border of each kidney is convex; the medial border is notched to form a slitlike opening, the *hilum*, through which vessels and nerves enter and leave the organ. The hilum leads into a wide space surrounded by the substance of the kidney, the *renal sinus*, in which the upper, expanded end of the ureter, the *renal pelvis*, is located. Besides the renal pelvis, with its terminal divisions or *calyces*, the sinus also contains branches of the renal arteries and veins, lymphatic vessels, fat and loose connective tissue, and nerves. Into it project the renal papillae.

THE CORTEX. The parenchyma of the kidney is divided into cortex and medulla. The cortex forms the peripheral portion of the kidney and lies between the medulla and the capsule. At intervals, portions of the cortex, known as the *renal columns of Bertini*, are prolonged downward through the entire width of the medulla. The uriniferous tubules are arranged in columns which extend from the medulla into the cortex, giving this portion of the cortex a striated appearance. These tubular columns are known as the *medullary rays (cortical rays; processes of Ferrein)* and the portion of the cortex which is occupied by the medullary rays is known as the *pars radiata*. Between the medullary rays the cortex has an irregular appearance due to the twisted course followed by the tubules of which its substance is composed. This part of the cortex is known as the *pars convoluta (cortical labyrinth)*. The numerous small, reddish, granulelike bodies, which

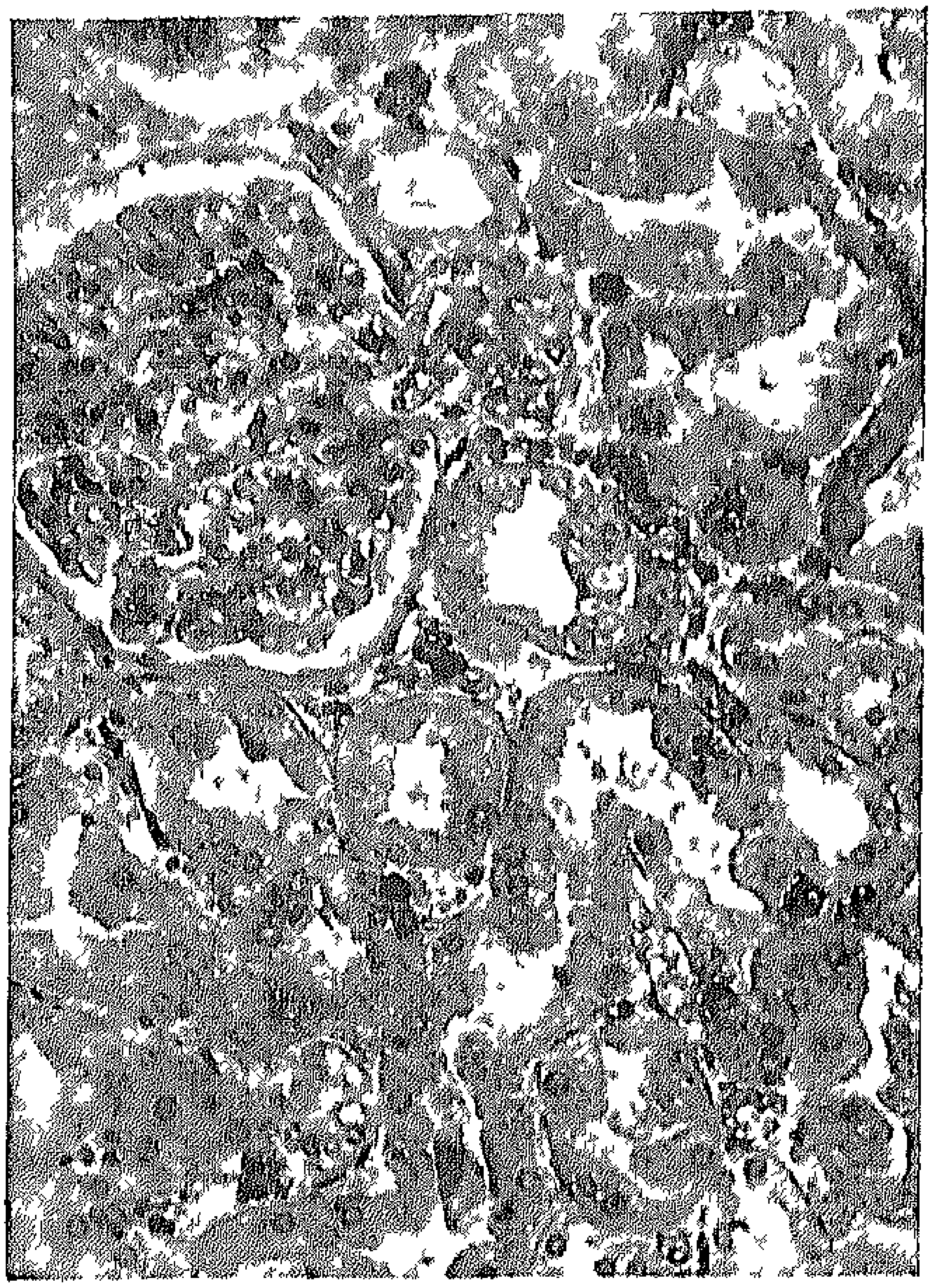


FIG. 181. Cortex of the kidney showing a glomerulus and its relation to the convoluted tubules. Photomicrograph

are to be seen in the convoluted portion of the cortex, are known as the *renal (Malpighian) corpuscles*.

THE MEDULLA. The medulla consists of a number of pyramidal structures, the *renal (Malpighian) pyramids*, of which there may be from eight to fifteen in a single kidney. Each pyramid presents a base and an apex. The base is directed peripherally and lies in contact with the cortex, while the apex or the *renal papilla* extends into the sinus. Occasionally the base of a pyramid may present a lobulated appearance, which indicates that two or more of the original lobules of the kidney have been united in a single structure. When the sectioned surface of a pyramid is examined with a magnifier, it presents a striated appearance due to the presence of a large number of tubular structures, the *uriniferous tubules*, of which the medullary substance is mainly composed.

RENAL PELVIS. The renal pelvis is divided into two or three prolongations, the *major calyces*, which are subdivided into a number of cup-shaped extensions, the *minor calyces*. There are usually about three major calyces which divide to form six to eight minor calyces. The renal papillae project into the calyces, the borders of which close about the external surfaces of the papillae. As a rule, a single papilla projects into a calyx; however, it is not unusual to find a single calyx containing two, or even three papillae. The connective tissue surrounding the wall of the renal pelvis contains the blood vessels and nerves which pass through the sinus to the substance of the kidney.

In some of the lower animals, such as the guinea pig, the kidney consists of a single pyramid surrounded by a peripheral layer of cortical material. A structure of this kind is regarded as constituting a single renal lobule. The human kidney is a combination of a number of such lobules, each of which is represented by a

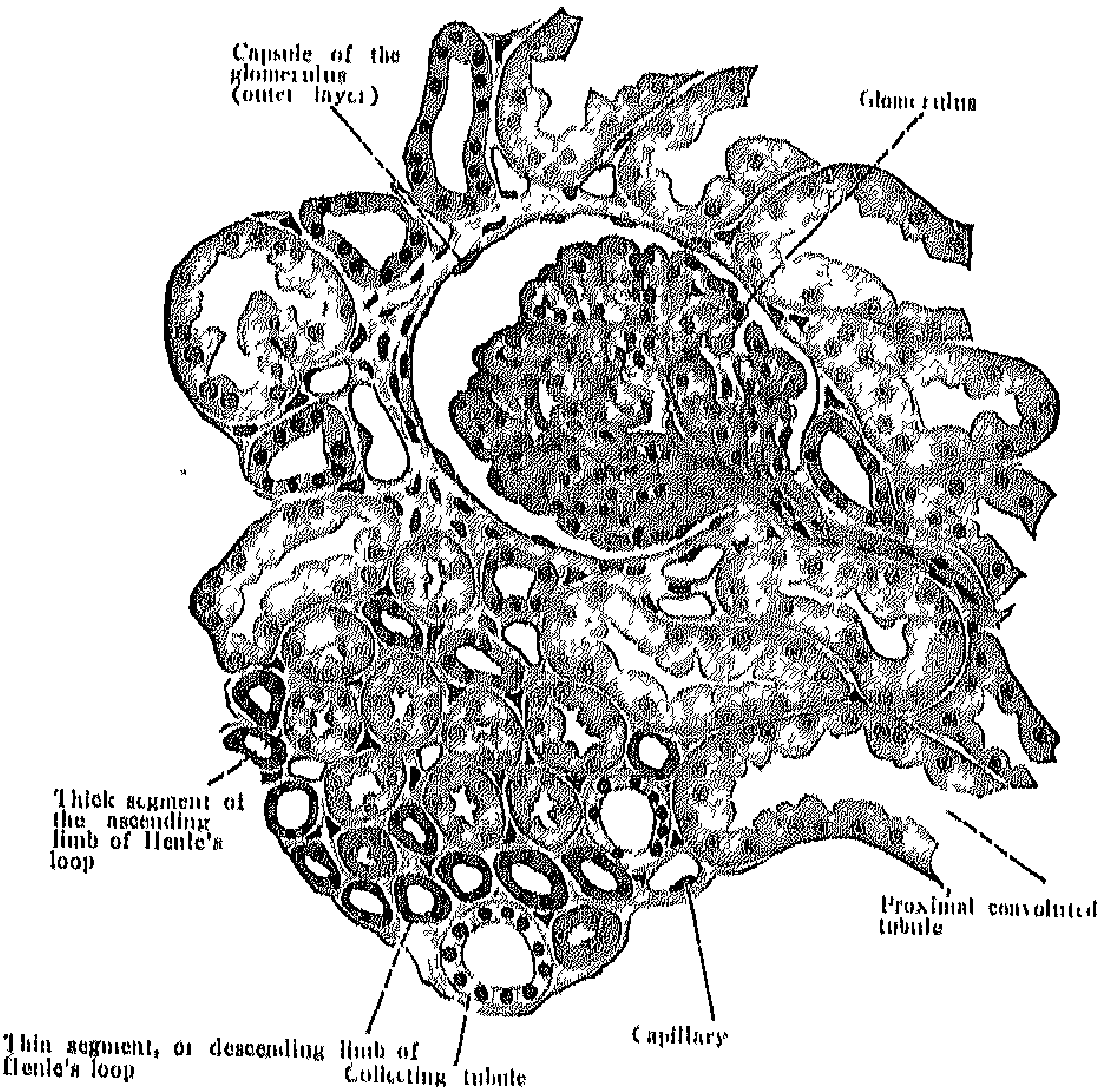
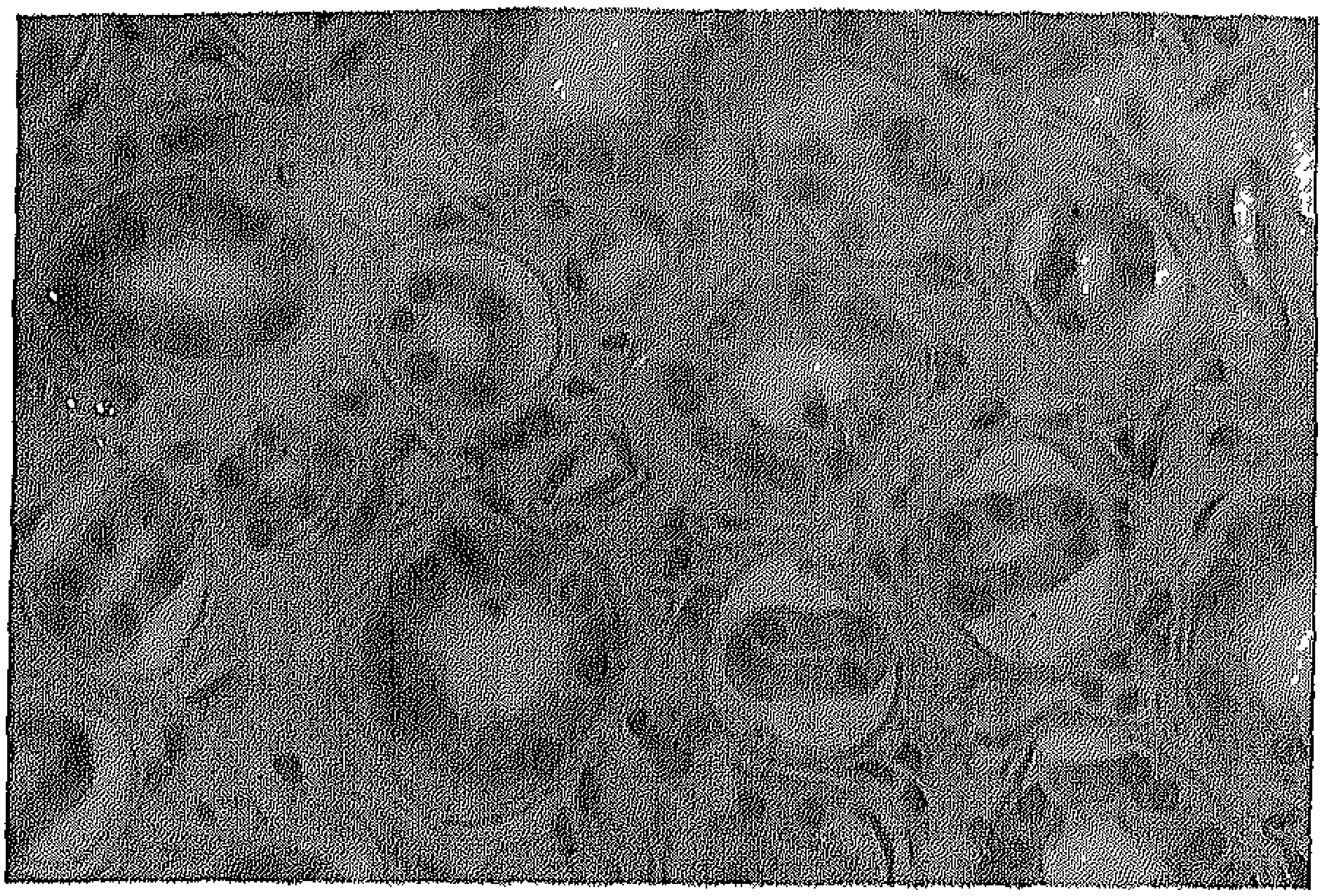

Capsule of the glomerulus (outer layer)
Glomerulus
Thick segment of the ascending limb of Henle's loop
Proximal convoluted tubule
Capillary
Thin segment, or descending limb of Henle's loop
Collecting tubule

FIG. 185. Tangential section of the cortex of a human kidney. 200 × (Schäfer.) The pars radiata is seen in the lower left corner. The line from "capsule of the glomerulus" passes between two distal convoluted tubules. (Courtesy, Bremer Weatherford, "Textbook of Histology," Philadelphia, The Blakiston Company.)

medullary pyramid. In the fetal kidney this arrangement is quite apparent, the lobules being well-defined by septa of connective tissue, which extend inward between them from the capsule. As development progresses, the substance of the kidney encroaches on the connective tissue which ultimately disappears, the lobulation of the kidney being apparent only by the presence of the pyramids and the arrangement of the blood vessels. Occasionally, however, the primitive lobulation of the kidney may persist in the adult structure.

RENAL CORPUSCLE. The Malpighian or renal corpuscle is a more or less spherical structure found in great numbers (estimations vary from 1–4.5 million in each kidney) in the convoluted portion of the cortex. The size of the corpuscles varies somewhat but the average diameter in man is nearly 200 microns. A renal corpuscle consists of two parts: a capsular part *(Bowman's capsule)* and a vascular part which consists of a tuft of capillaries, the *glomerulus*. Each renal corpuscle has a vascular pole, where the glomerular vessels enter and leave, and nearly opposite it is the urinary pole where the capsule is continued into the neck of the uriniferous tubule. The glomerular capsule consists of an inner visceral portion and an outer parietal portion. The visceral layer is composed of a layer of very flattened epithelial cells which are so intimately applied to the glomerulus that it is practically impossible to distinguish the capsular cells from the endothelial cells lining the capillary tufts. This epithelium completely covers the glomerulus and at the vascular pole it is reflected back on itself as the parietal layer. It is relatively easy to make out the cells forming the parietal layer. They are flattened like the cells of the visceral layer, but as the urinary pole is approached these cells become thicker and gradually assume a low columnar shape as they become continuous with the cells lining the neck portion of the uriniferous tubule. The epithelial cells lining the capsule rest on a thin, clear, homogeneous basement membrane. Between the visceral and the parietal layer is a space which is continuous with the lumen of the proximal convoluted tubule.

The blood vessels forming the glomerulus consist of a number of distinct and separate vascular loops. Blood is brought to the glomerulus by the *afferent artery* which enters the renal corpuscle at its vascular pole. This vessel breaks up into a number of capillary-like vessels which lie within the visceral layer of the capsule and form the glomerulus. After winding about in a series of distinct and separate loops, these capillaries unite to form the *efferent artery* through which the blood leaves the glomerulus. The efferent artery also leaves the glomerulus at the vascular pole. The efferent artery is smaller than the afferent artery, a condition which aids in increasing the pressure of the blood in the capillary loops. The blood which enters the capillary loops of a glomerulus retains its arterial properties and leaves the



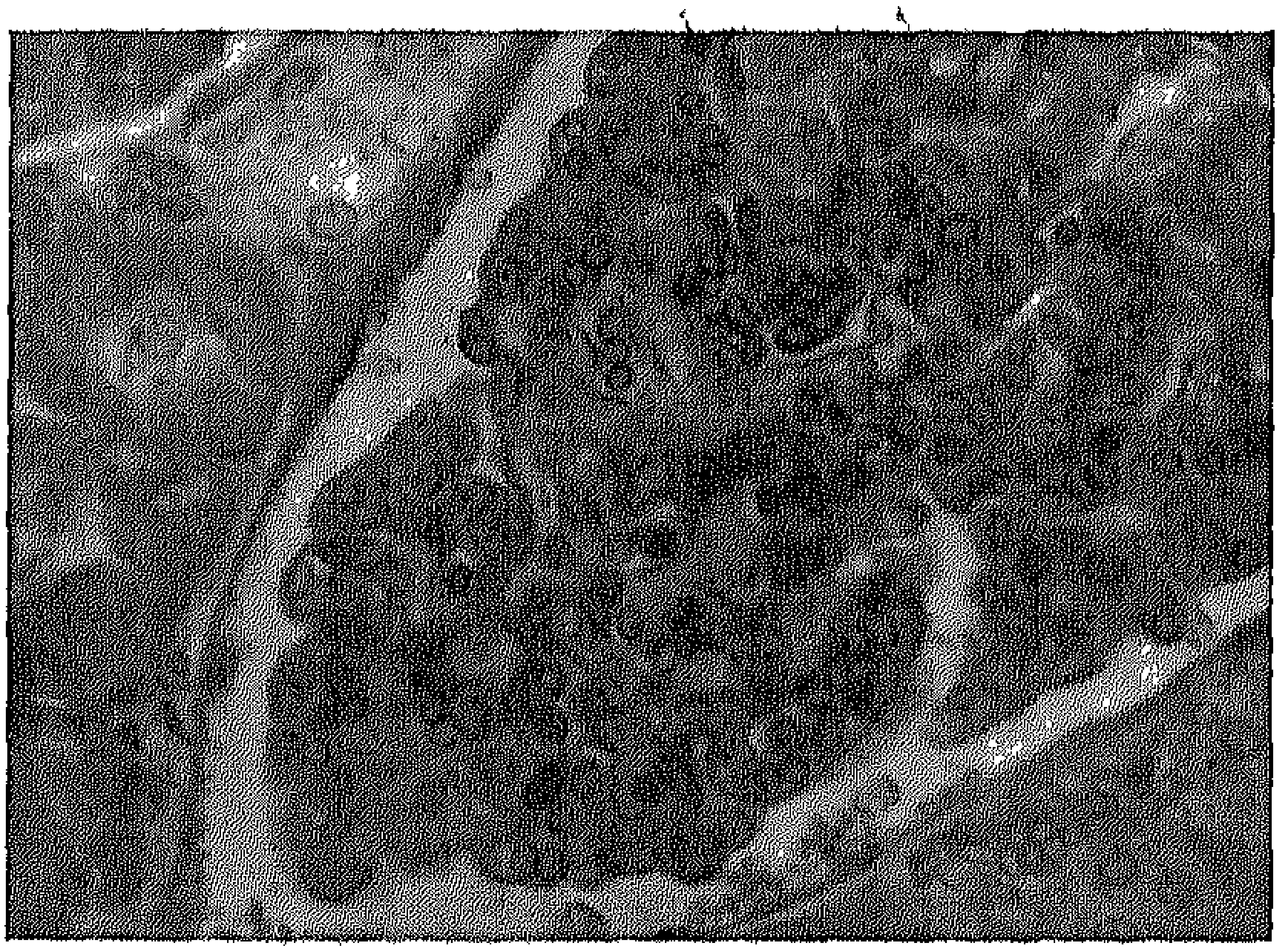


FIG. 186. Transverse section through the medulla of a human kidney. Photomicrograph.

FIG. 187. Portion of a glomerulus (highly magnified) showing the capsule of Bowman, and a proximal convoluted tubule. (Note the brush borders on these cells.) Photomicrograph.

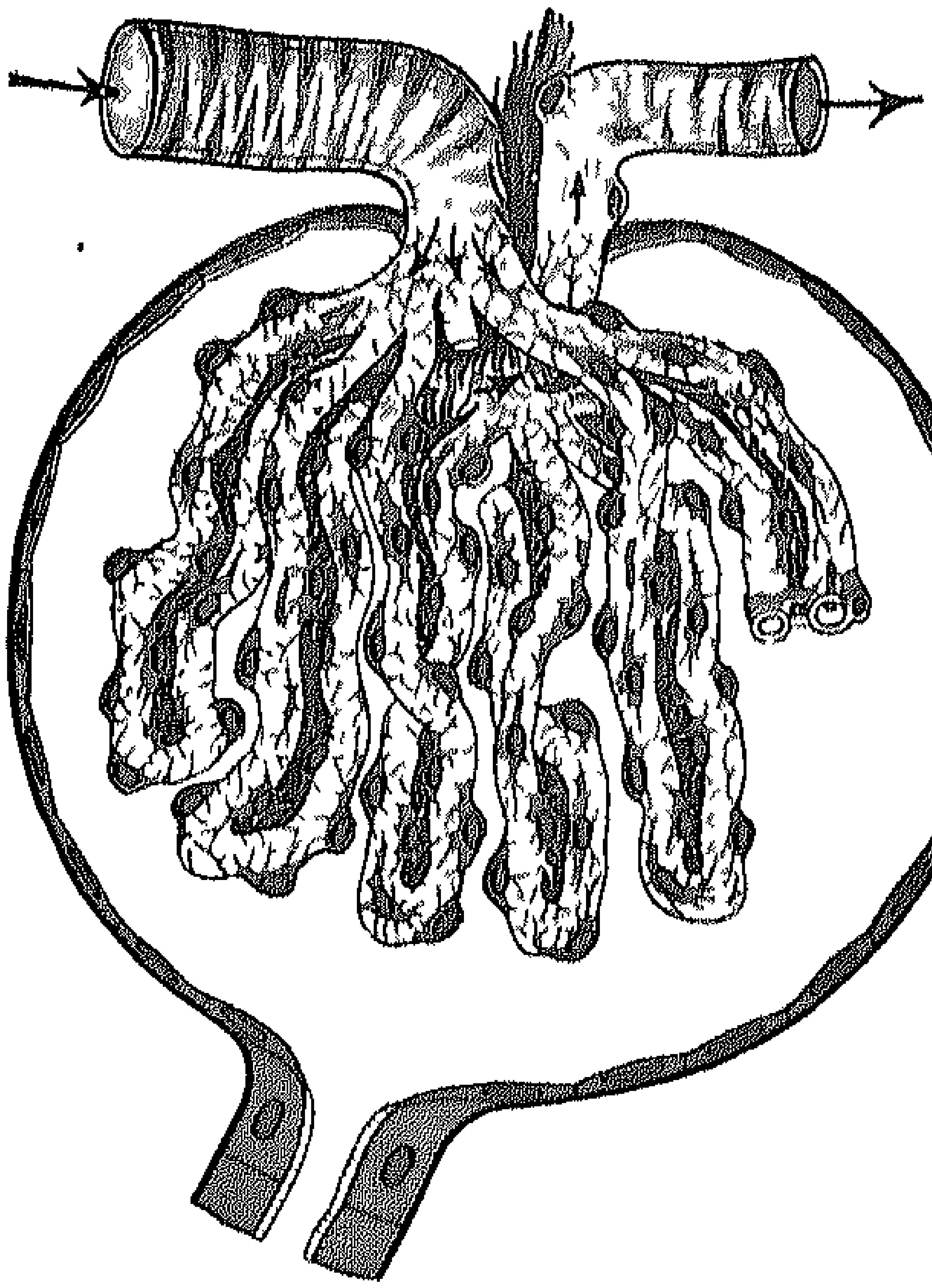


FIG. 188. A diagrammatic representation of a renal corpuscle in which the number of capillary loops is reduced for clearer illustration. (von Mollendorff.) (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

glomerular area as arterial blood. Therefore, a glomerulus should not be regarded as a set of capillaries, but as small arterial vessels. The blood which has passed through the glomerulus does not become venous until it has accomplished its exchange of gases in the capillaries which wind about the tubules. Structurally the afferent and efferent arteries resemble arterioles. Near the glomerulus, however, the wall of the afferent vessel contains a specialized myoepithelial cell which either overlays the circular layer of muscle or may replace it. These cells have homogeneous pale staining cytoplasm. As the afferent vessel enters the glomerulus these cells form a band around the vessel known as the *juxtaglomerular apparatus*. Its function is unknown but it has been suggested that these cells may produce an endocrine secretion effecting constriction of the vessel walls.

URINIFEROUS TUBULES. The uriniferous tubules form the major part of the parenchyma of the kidney. They are surrounded and supported by small quantities of interstitial connective tissue in which

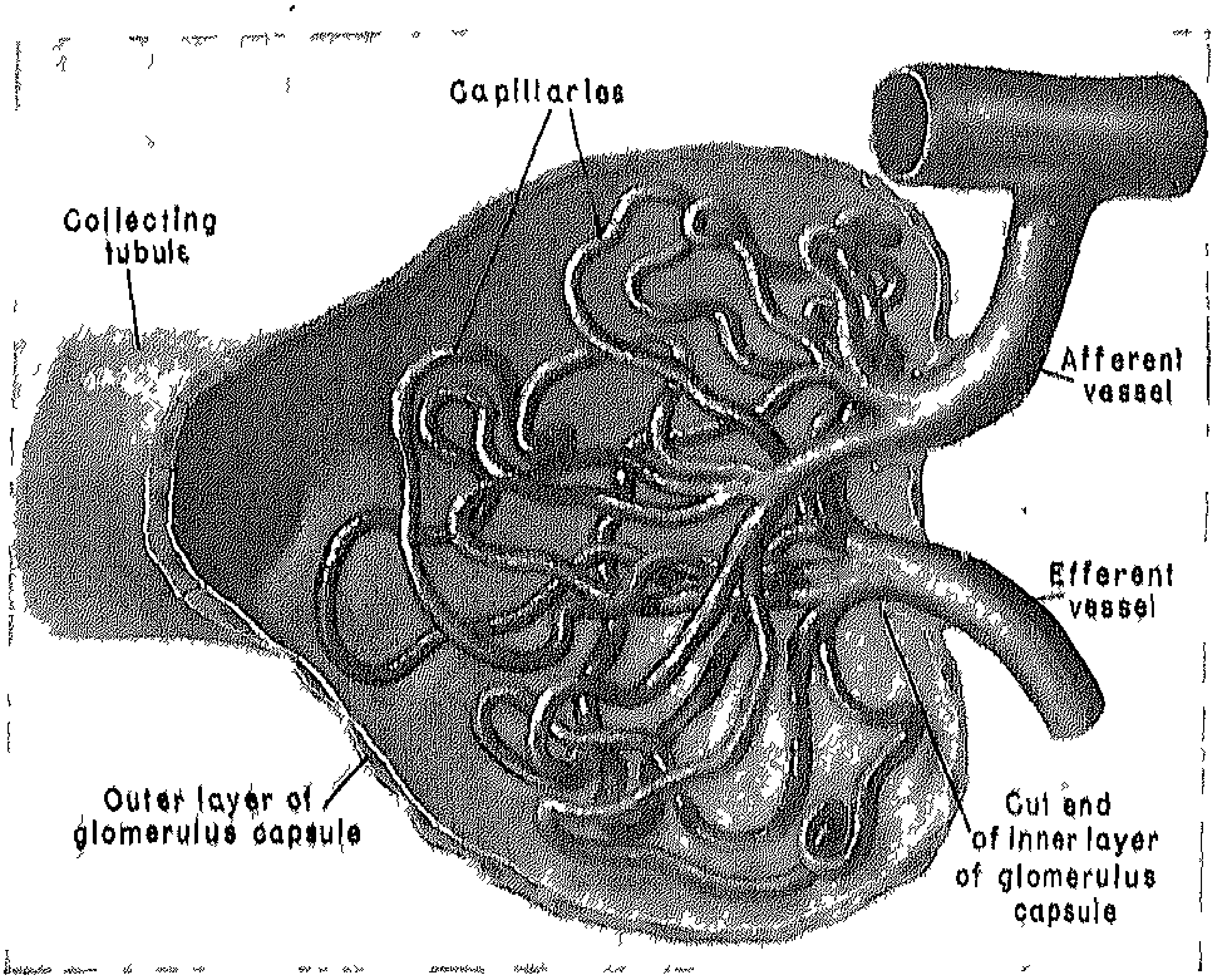

Capillaries
Collecting tubule
Afferent vessel
Efferent vessel
Outer layer of glomerulus capsule
Cut end of inner layer of glomerulus capsule

FIG. 189. Diagram to show the arrangement of capillary loops in a glomerulus. Note absence of anastomoses between loops.

run blood vessels, lymph vessels and nerves. Two types of tubules are recognized: the *secretory* or *terminal tubules* which produce the urine, and the *collecting tubules* which carry it to the ureter. The terminal tubules begin in the expanded portion made up of a capillary tuft with its enclosing capsule, known as the *renal* or *Malpighian corpuscle*. From the corpuscle the terminal tubules run a tortuous course to their termination with the collecting tubules. These terminal tubules are made up of a number of successive segments, each of which occupies a definite position in relation to the renal corpuscle and has its own particular type of epithelial cell lining it. The tubules of each segment differ in length and diameter from those in other segments. These secretory tubules represent both the structural and physiological unit of the kidney and are known as the *nephron*. Named in order, the successive segments of a nephron are: the renal corpuscle, proximal convoluted tubule, descending limb of Henle's loop, loop of Henle, and ascending limb of Henle's loop, and the distal convoluted tubule. The excretory portion of the tubules follows next and the segments are: the arched tubule and the collecting tubules. Attention should be called to the fact that the secreting tubules really are not "glandular" in function, since they fail to synthesize any urinary constituent, the elements of which are not already present in the blood stream.

SECRETORY PORTION OF URINIFEROUS TUBULE. The active or secretory part of the uriniferous tubule begins with the renal corpuscle and ends with the distal convoluted tubule. At the point where the capsule of the renal corpuscle is continued into the proximal convoluted tubule there is a constricted portion called the *neck*. The proximal convoluted tubules occupy the greater part of the pars convoluta of the cortex. They are the widest (40-60 microns) as well as the longest part of the nephron. A proximal convoluted tubule begins at the neck, by which it is joined to the capsule and following a somewhat twisted course, describes a loop toward the periphery of the cortex. Returning to the point near the corpuscle from which it started, it enters the nearest medullary ray in which it passes downward toward the pyramid.

The epithelium of the proximal tubules consists of large, pyramidal cells which rest on a clear, homogeneous basement membrane. The boundaries of these cells are not apparent in ordinary sections. The cells of this segment are difficult to see clearly. They are readily affected by post-mortem changes and by the physiological activity of the organ. In silver nitrate preparations they are seen to have deeply serrated, interdigitating borders. During periods of rest the cells are tall and encroach on the lumen, which is narrow and irregular. After a period of active secretion the cells are lower and the lumen wider. The spherical nuclei are located toward the basal portions of the cells, which present a striated appearance due to the presence of rows of granules. Mitochondria are also present and are arranged in the form of rows extending from the basal portion of the cell for a variable distance into the cytoplasm. During diuresis the rodlike mitochondria become granular in appearance. A Golgi apparatus may also be present. The free borders of the epithelial cells in the proximal tubules have a finely striated appearance. This is due to the presence of delicate, protoplasmic filaments which, under ordinary magnifications give the cells the appearance of being ciliated, and which are collectively known as a *brush border*. The brush border has been described as a cuticular plate, pierced by numerous, minute channels through which protoplasmic processes extend toward the surface. These cells degenerate rapidly after death has occurred *(autolysis)* so that, in the majority of preparations, the brush border has been destroyed. When the epithelial tissue is only mildly autolyzed, the substance between the filamentous processes is destroyed. The processes, however, remain and have the appearance of cilia. No other cells in the kidney have a brush border.

The proximal tubule extends downward for some distance in the medullary ray, then by an abrupt change in its diameter and in the character of its epithelium it becomes the *descending limb of Henle's loop.* The descending limb continues into the pyramid where it bends sharply on itself and returns to the convoluted portion of the cortex as the *ascending limb.*

Henle's loop consists of a thin segment and a thick segment. The thin segment, which is the narrowest part of the nephron, has a diameter of 12-15 microns. Its epithelium consists of flattened cells with large oval nuclei which, because of their size, cause a considerable bulging of the cellular cytoplasm. The cytoplasm of these cells is clear and any attempt to demonstrate protoplasmic granules or granules of mitochondria have failed. The thin segments are frequently mistaken for capillaries, although the cells which form their epithelium are considerably thicker than the endothelial cells of the capillary walls. The diameter of the thick segment is about twice that of the thin segment; the change from the thin to the thick segment takes place abruptly, usually in the descending limb, although it may not occur until after the turn of the loop has been passed, in which case a considerable portion of the thin segment is included in the ascending limb. The epithelium of the thick segment consists of cuboidal cells with round, centrally located nuclei. Between the nucleus and the lumen, the cytoplasm is clear and there is no brush border. The basal area of the cells appears striated due to the vertically arranged rows of granules. During diuresis no change occurs in the appearance of the cells. Granular mitochondria are found in the cytoplasm toward the free surfaces of the cells. A Golgi apparatus may also be present.

The distance to which the loop of Henle descends in the medulla depends on the position of the renal corpuscle, from which it takes its origin in the cortex. When the corpuscle lies close to the medulla, the loop extends deeply into the pyramid and may even reach the papilla. Loops which arise from corpuscles in the more peripheral portions of the cortex are likely to descend into the medulla for only a short distance. Occasionally a loop may be so short that it fails to reach the medulla. In returning to the convoluted portion of the cortex, the ascending limb of Henle's loop comes into relation with that part of its corpuscle which receives the afferent artery. It then bends around the corpuscle and ends in the *distal convoluted tubule.*

The distal convoluted tubule pursues a less tortuous course. Its coils lie, for the most part, within the loop formed by the proximal tubule. Its epithelium consists of cells which are, at first, cuboidal, but they gradually increase in height until they have attained a columnar or pyramidal form. Except for the change in height, these cells are similar in appearance to the cells lining the thick segment of Henle's loop. Basal striations are present but are not as clearly defined as in the cells of the proximal tubules. The cells of the distal tubules do not possess a brush border. Since the epithelium is lower in the distal tubules than in the proximal tubules, the lumen is relatively wide.

EXCRETORY PORTION OF URINIFEROUS TUBULES. The conveying or excretory portion begins with the arched tubule and includes the collecting tubules and papillary ducts. The *arched* or *junctional tubule* lies in the convoluted portion of the cortex and is continuous with the straight collecting tubule. It is somewhat smaller than the distal convoluted tubule and is lined by an epithelium consisting of cuboidal cells which have a clear cytoplasm and spherical, deeply staining nuclei. It joins with a number of similar tubules to form the first and smallest of the collecting tubules (*straight collecting tubules*).

The straight collecting tubules begin in the medullary rays, where the larger are formed by the union of the smaller tubules. This is repeated several times until the tubules which pass from the medullary rays into the pyramids have increased considerably in size, but have been reduced in number.

The tubules which are seen in sections of the medulla are arranged in groups, each group including those which have been formed in a single medullary ray. Mingling with the groups of collecting tubules, are sections of the descending and ascending limbs of Henle's loops. The epithelium lining the smaller tubules consists of cuboidal cells which enclose a wide, definitely outlined lumen and possess a clear cytoplasm and deeply staining, spherical nuclei. With the increase in the diameter of the tubules there is an increase in the height of the cells which form their epithelium, until, in the larger tubules, they are definitely columnar.

By the repeated unions of the collecting tubules, a single, large *papillary duct (duct of Bellini)* is formed. A single papilla contains from 10–20 papillary ducts which open into a calyx through apertures known as the *papillary foramina*. On the apex of the papilla, the area in which the papillary foramina are located is called the *area cribosa*. The papillary ducts are the largest of the tubules and have a diameter of 200 microns or more. Their epithelium, which consists of columnar cells, passes through the foramina and is continuous with the modified transitional epithelium covering the external surface of the papilla.

A small amount of interstitial connective tissue is present between the tubules and serves to bind them together. There is less interstitial tissue between the tubules in the cortex than in the medulla. It is more abundant in the renal papilla, between the ducts of Bellini, than elsewhere in the kidney.

BLOOD SUPPLY. Blood passes to the kidney through the *renal artery*, which is a branch of the aorta. The artery breaks up in the renal sinus into a number of branches which pass as the *interlobar* *arteries*, between the cortical columns and the medulla. Before leaving the sinus these vessels give off a number of twigs which supply the wall of the renal pelvis and the capsular connective tissue. On reaching the line of separation between the medulla and cortex, the interlobar vessels take a sharp turn, passing over the bases of the pyramids in the incomplete septa of connective tissue which lie between the pyramids and the cortex. These vessels are known as the *arcuate*, or *arciform arteries*. Branches from the arcuate arteries extend perpendicularly through the cortex and end in a network of capillaries just beneath the capsule. These branches are known as the *interlobular arteries*. Some of the terminal branches of the interlobular arteries continue into the capsule where they anastomose with the capsular branches of the renal artery. The interlobular arteries give off lateral branches which become the *afferent arteries (vasa afferentia)* of the glomeruli. After passing through the vascular loops of the glomeruli, the blood leaves the capsule through the smaller *efferent arteries (vasa efferentia)*, which form rich capillary networks about the tubules in the pars convoluta of the cortex. Some of the branches from the efferent arteries also supply the tubules in the medullary rays. The medulla is supplied by vessels which arise as branches of the efferent arteries (possibly from the afferent arteries as well) of those capsules which lie nearest the border of the medullary area. These vessels pass directly downward into the medulla and are known as the *arteriae rectae*. They end in capillaries which form networks about the medullary tubules.

After coursing through the capillaries, which are formed by the end branches of the renal vessels, the blood enters the veins. In the periphery of the cortex, several of these veins converge upon a series of common trunks forming radial, or starlike, arrangements. These converging vessels are known as the *stellate veins of Verheyens*. The trunks formed by the convergence of the stellate veins pass downward in the cortex as the *interlobular veins*, and after receiving numerous lateral branches in their course, they join the *arcuate veins*. Following the course of the arcuate arteries, the arcuate veins become the *interlobar veins* and reach the renal sinus where they unite to form the *renal vein*, which leaves the kidney in company with the renal artery and the ureter at the hilum. The arcuate veins receive branches which arise in the cortex, as well as veins *(venae rectae)* which pass upwards in the pyramids, to return the blood from the capillaries about the medullary tubules.

LYMPHATIC SUPPLY. The kidney is well supplied with lymphatics. The principal (deep) lymphatics arise from capillary networks about the convoluted tubules. These vessels unite in branches which follow the course of the arteries and veins to the sinus where they join the lymph trunks leaving the kidney at the hilum. A secondary (superficial) group consists of lymph vessels in the capsule, which join the extrarenal lymphatics.

NERVE SUPPLY. The nerve supply of the kidney is principally by unmyelinated fibers from the coeliac plexus which is a part of the autonomic system. The nerves follow the course of the blood vessels to the renal corpuscles and then pass to the convoluted tubules where some of the fibers end on the basement membrane. Other fibers penetrate the membrane and appear to end in relation to the cells of the epithelium. Unmyelinated fibers also end in the walls of the blood vessels. Myelinated fibers, probably sensory, can be traced to the walls of the renal pelvis and also appear to end in the capsular connective tissue

THE URETER

After it has been excreted by the kidney, the urine is conveyed to the bladder by a long, narrow tube, the *ureter*. The ureter begins as the renal pelvis with its subdivisions, the major and minor calyces. Shortly after leaving the hilum of the kidney it narrows to form a tubelike structure which continues to its junction with the bladder.

The general structure of the ureter is the same in all its parts.

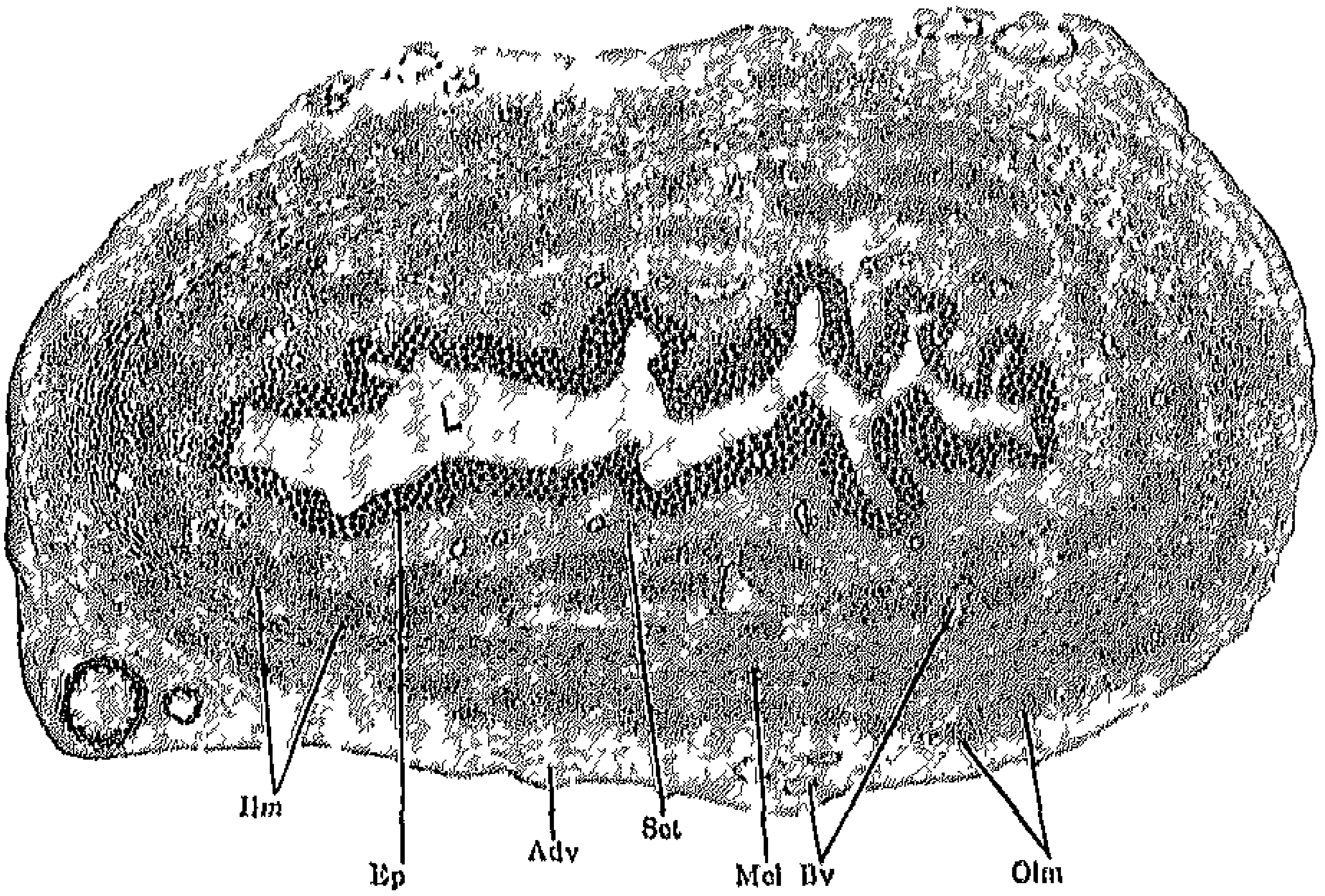


FIG. 190. Section through a ureter (human). (L) Lumen. (Ep) Transitional epithelium. (Sct) Sub-epithelial connective tissue (stroma). (Ilm) Inner layer of longitudinal muscles. (Mcl) Middle circular muscle layer. (Olm) Outer layer of longitudinal muscles (Adv) Adventitia. (Bv) Blood vessels.

Its wall consists of three layers or coats: a *mucous coat*, a *muscular coat*, and a *fibrous coat* or *adventitia*.

The *mucous coat* consists of an epithelium and a layer of subepithelial connective tissue, or stroma. The epithelium, which is the stratified form commonly known as "transitional," is two or three layers of cells in depth where it lies on the surfaces of the papillae and lines the calyces. It is four to six cell-layers in depth where it lines the renal pelvis and the upper part of the ureter, and has a depth of six to eight, or more, cell layers in its lower half. In transitional epithelium, the cells of the basal row are cuboidal or low columnar. Those of the intermediate rows are polyhedral, while those of the surface layer are cuboidal, but become flattened when the walls of the ureter are distended. The deep surfaces of the superficial cells are indented to receive the rounded portions of the pear-shaped cells of the subjacent row. The connective tissue, or stroma, on which the epithelium rests (a basement membrane is not visible), consists of delicate collagenous fibers with which a few elastic fibers are intermingled. The tissue is loosely arranged, and in places assumes a reticular form with many lymphocytes present. Lymphoid tissue may be in the form of small nodules, particularly in the region of the calyces. No true glandular structures are present, although there are certain downgrowths of the epithelium which are regarded as vestigial glands, although they do not, as a rule, possess lumina.

The *muscular coat* consists of smooth muscle fibers arranged as an inner longitudinal and an outer circular layer. In the lower half of the ureter a third layer, in which the fibers are longitudinally or obliquely directed, lies external to the circular layer. The longitudinal and circular layers are well developed in the renal pelvis. The circular fibers are strengthened where the calyces are arranged about the papillae, forming a sphincterlike arrangement. In the upper half of the ureter, the inner longitudinal muscles are in scattered bundles while in the lower half the longitudinal muscles form a more definite layer. All three layers of the ureter extend into the wall of the bladder where they become more or less interwoven.

The *adventitia* is a layer of fibroelastic tissue which forms the outer coat of the wall of the ureter. Close to the muscular coat, the fibers are condensed to form a firm investment for the ureter, external to which the adventitia gradually merges in the loose areolar tissue with which the tube is surrounded and by which it is attached to adjacent structures. As the ureter penetrates the wall of the bladder, the adventitia forms a firm outer covering, separating it from the tissues of the bladder wall by which it is surrounded.

BLOOD AND LYMPHATIC SUPPLY. The blood supply is from a series of vessels which penetrate the wall of the ureter and form capillary networks about the muscle bundles and in the mucous coat in which these capillary networks are especially developed immediately beneath the epithelium.

The lymphatics arise principally in the region of the muscular tissues, although a few lymphatic vessels are present in the mucous coat and in the adventitia. The vessels which these lymphatics form, drain into small, adjacent lymph nodes.

NERVE SUPPLY. The nerves consist of unmyelinated fibers from the autonomic system, which pass to the muscle bundles and to the walls of the blood vessels and myelinated fibers, probably sensory, that end in the tunica propria and between the cells of the epithelium.

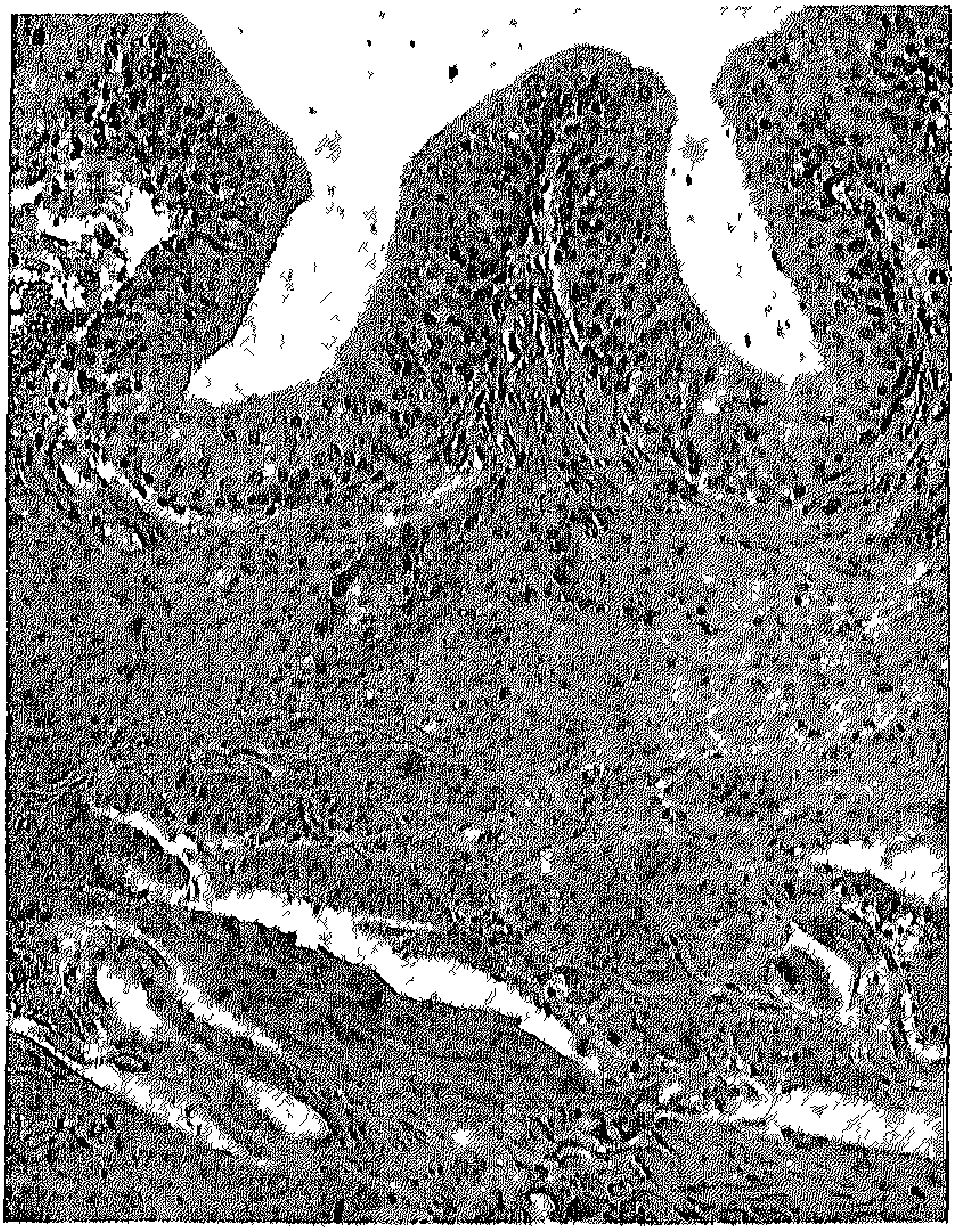


FIG. 191. Partial section of tangential cut through a ureter. Photomicrograph.

THE BLADDER

The bladder is a large, muscular sac which receives the urine and retains it until it is eliminated from the body. It consists of a rounded portion, the *fundus;* the *body,* which constitutes the greater portion of the organ; and a thickened, triangular area, the *trigone.* The base of the trigone is between the ureters as they enter the bladder, the apex being at its urethral outlet. Structurally, the walls of the fundus and body are the same. Due to a marked increase in its muscular coat, the wall of the trigone is considerably thicker.

The wall of the bladder includes: a *mucous coat,* a *stroma,* a *muscular coat* and an *adventitia.*

The *mucous coat* consists of a layer of transitional epithelium and a subepithelial layer of delicate reticular tissue containing many lymphocytes. No definite basement membrane is present in connection with the epithelium of either the bladder or ureter. When the bladder wall is strongly contracted, the epithelium appears to be several cell layers in depth, the form and arrangement of the cells being the same as in the epithelium of the ureter. When the bladder wall is distended, the cells become thin and flattened consisting of only two or three cell layers. It is claimed that when the wall of the bladder is distended, the epithelial cells are not only stretched and flattened, but that they also slip over one another, a condition made possible by the soft, yielding character of the intercellular cement.

The *stroma,* upon which the epithelium of the bladder rests, consists of two parts. The part which lies immediately beneath the epithelium consists of delicate fibers arranged in the form of a reticulum. Elastic fibers are scattered throughout this layer and lymphocytes, occasionally aggregated in the form of small nodules, are also present. This part of the subepithelial tissue, which is commonly referred to as the tunica propria, gradually merges into the second part which consists of coarser fibers and is known as the submucosa. A submucosa is not present in the trigone, the muscular coat lying directly in contact with the mucosa.

True glandular structures are not present in the fundus or body of the bladder. Pocketlike downgrowths of the epithelium occur and may, or may not, possess a lumen. When a lumen is present, it is usually filled with a substance called *colloid.* These structures, which are regarded as vestigial glands, are somewhat larger in the trigone and about the urethral opening, where they give rise to a number of branched tubular structures lined by a columnar epithelium, and are thought to indicate a former attachment of the prostate to this portion of the bladder.

The *muscular coat* is relatively thick, consisting of bundles of

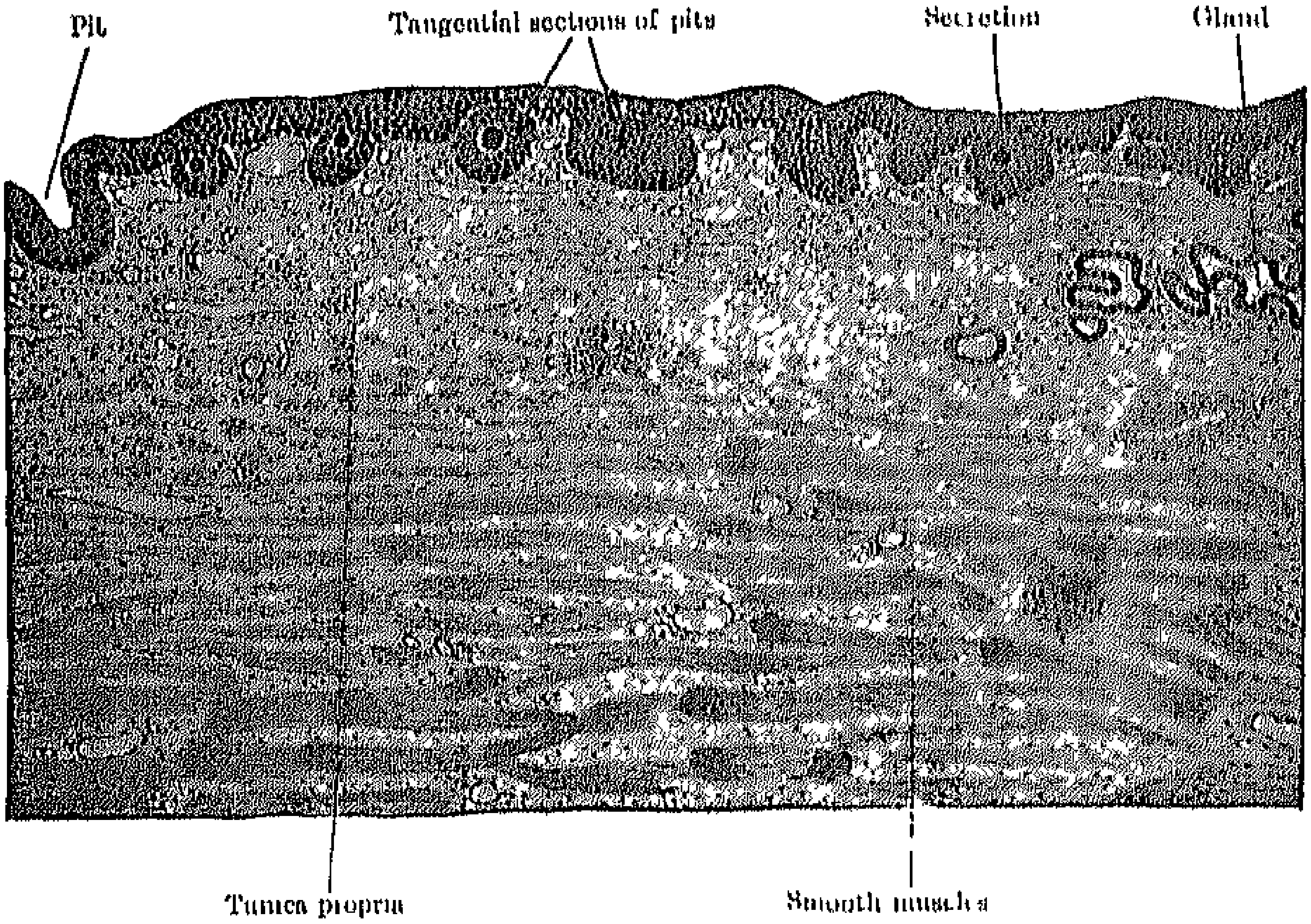


FIG. 192. Section through the fundus of the urinary bladder of an adult man. 48 × (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

smooth muscle fibers arranged in an inner longitudinal layer, a middle circular layer and an external layer in which the fibers are also longitudinally directed. The bundles which form the inner layer are more or less scattered, being separated by the fibers of the submucosa which extend between them. The circular layer is the most strongly developed of the three, while the outer layer is quite thin and is poorly developed, except in the trigone. The three layers encroach more or less on one another and, therefore, are difficult to distinguish in sections.

The *adventitia* is a layer of loosely arranged areolar tissue. It blends with the connective tissue of the peritoneum which extends over the wall of the bladder and forms a serous coat on its upper and lateral surfaces. On the remaining surface it is a part of the connective tissue by which the bladder is attached to the pelvic wall.

BLOOD AND LYMPHATIC SUPPLY. The blood supply of the bladder is similar to that of the ureter. The principal vessels form a network in the connective tissue covering its surface. The branches of this network penetrate the wall of the bladder and form a capillary plexus about the muscle bundles and in the tunica propria immediately beneath the epithelium.

The lymphatics originate as capillaries in the muscular layers and form vessels which drain into the nearest lymph nodes.

CHARACTERISTICS OF THE SEGMENTS OF A URINIFEROUS TUBULE

	Diameter in micra	*Length in mm.*	*Epithelium*	*Location*	
Malpighian corpuscles (Bowman's capsule)	200		Flattened	Pars convoluta (cortex)	Secretory portion
Proximal convoluted tubule	57-60	14	Low columnar or pyramidal Brush border Basal striations	Pars convoluta (cortex) Pars radiata (cortex) Outer zone (medulla)	
Descending limb of Henle's loop (thin segment)	15	Variable	Flattened cells	Outer zone (medulla) Inner zone (medulla)	
Ascending limb of Henle's loop (thick segment)	30	9	Simple cuboidal Basal striations less distinct than in distal convoluted tubule	Pars convoluta (cortex) Pars radiata (cortex) Outer zone (medulla)	
Distal convoluted tubule	20-50	4-5	Simple cuboidal No brush border Faint basal striations	Pars convoluta (cortex)	
Arched collecting tubule			Simple cuboidal	Pars convoluta (cortex)	Excretory portion
Straight collecting tubule	40	20-23	Simple cuboidal to columnar	Pars radiata (cortex) Outer zone (medulla) Inner zone (medulla)	
Papillary ducts	100-200	30-40	Simple columnar	Inner zone (medulla)	

NERVE SUPPLY. The nerve supply is by unmyelinated fibers, which end in relation to small groups of ganglion cells in the fibrous tissue. The processes from these cells extend to the muscular layers or end in the walls of blood vessels. Myelinated fibers end in relation to ganglion cells in the stroma, or as free fibers between the cells of the epithelium.

THE URETHRA

Because of the structural and functional relation of the male urethra to the organs of reproduction, and of the structural relation of the female urethra to the vagina, they will be discussed in connection with those organs.

18

The Ductless Glands

The *ductless* or *endocrine* glands differ from the exocrine glands in not possessing a system of ducts for the removal of their secretion, rather the substances they produce pass directly from the cells to the blood stream. The substances produced by the ductless glands are called *hormones*. They affect the metabolism and growth of the body through their influence on the functional activity of its organs.

The principal ductless glands are: the *islands of Langerhans* in the pancreas, the *thyroid*, *parathyroid*, *hypophysis* and *adrenal*. In addition, the follicles and corpora lutea of the ovary, the interstitial cells of the testis and the chorionic cells of the placenta produce important hormones. It is believed that the paraganglia are related to the adrenal medulla. Certain other structures such as the pineal, carotid and coccygeal bodies commonly are discussed under the heading of endocrine glands, but their function as such is questionable.

The ductless glands vary in their structural form and in the nature of the substances they produce. The epithelioid cells may be arranged in cords and masses in close relation to thin-walled capillary sinusoids, as in the islands of Langerhans or parathyroid; they may be in the form of follicles as in the thyroid gland and the intermediate lobe of the hypophysis; or they may appear as groups of cells which are apparently unrelated to the structures in which they occur, as the interstitial cells of the ovaries and testes.

THE ISLANDS OF LANGERHANS

For the discussion of the islands of Langerhans, see page 286.

THE THYROID GLAND

The thyroid originates from epithelioid cells which form a tubular downgrowth from the anterior portion of the pharynx. This tubular structure develops lateral extensions which come into contact with the ventral wings of the fourth branchial pouch. Although some observers claim that the latter form the lateral lobes of the thyroid, the evidence for this is not entirely satisfactory. As development progresses, the tubular downgrowth (*thyroglossal duct*) becomes obliterated. Its position in relation to the tongue is indicated by a pitlike depression, the *foramen caecum*, just behind the apex of the V-shaped row of circumvallate papillae. Small masses of thyroid tissue, called accessory thyroids, occasionally occur along the course of the obliterated duct.

The *epithelioid cells of the thyroid are first arranged as cords*, which develop anastomosing branches and form a network, the meshes of which are filled with connective tissue and numerous blood capillaries. As the development of the thyroid progresses, the epithelial cords are broken up into segments, each segment enlarging and acquiring a lumen, thus becoming one of the follicular structures of the gland.

Grossly the thyroid gland is seen to be roughly U-shaped and consists of two laterally placed *lobes* connected by a narrow strip called the *isthmus*. A median lobe may be present and it arises from the superior margin of the isthmus or from one of the lateral lobes. The deep cervical fascia of the neck splits to enclose the gland in a dense connective tissue sheath. Beneath this is another connective tissue layer which represents the real capsule of the gland. It consists of a thin, translucent layer of connective tissue from which delicate septa extend into the substance of the gland, dividing it into primary and secondary lobules. *Each primary lobule consists of a number of follicles grouped* together and separated from other similar groups by thin partitions of connective tissue. The size of the thyroid gland is extremely variable. The appearance of the follicles composing the gland also differs under certain conditions. The most marked changes in the gland occur in response to differences in iodine content of food. Sex, age, seasons and temperature also affect it.

The follicles which are the structural units of the thyroid gland vary considerably both in shape and size, some being microscopic in size and almost round, others elongated and cylindrical.

The follicular wall consists of a single row of cells. These vary in height from low cuboidal or even squamous to tall columnar, depending on the activity of the follicle. When the follicle is distended with colloid the cells are thin and flattened; however, when the cells are very active and storage of colloid is minimal, they appear tall columnar. In the normal thyroid where production, storage and release of *hormone are in equilibrium, the cells usually are cuboidal and have* a granular cytoplasm with small, round, vesicular nuclei. They possess both mitochondria and a Golgi apparatus which varies in appearance with the activity of the cells. These cells do not rest on a basement membrane, but are in immediate contact with the capillaries and interstitial tissue. The follicular cells are functionally bipolar, that

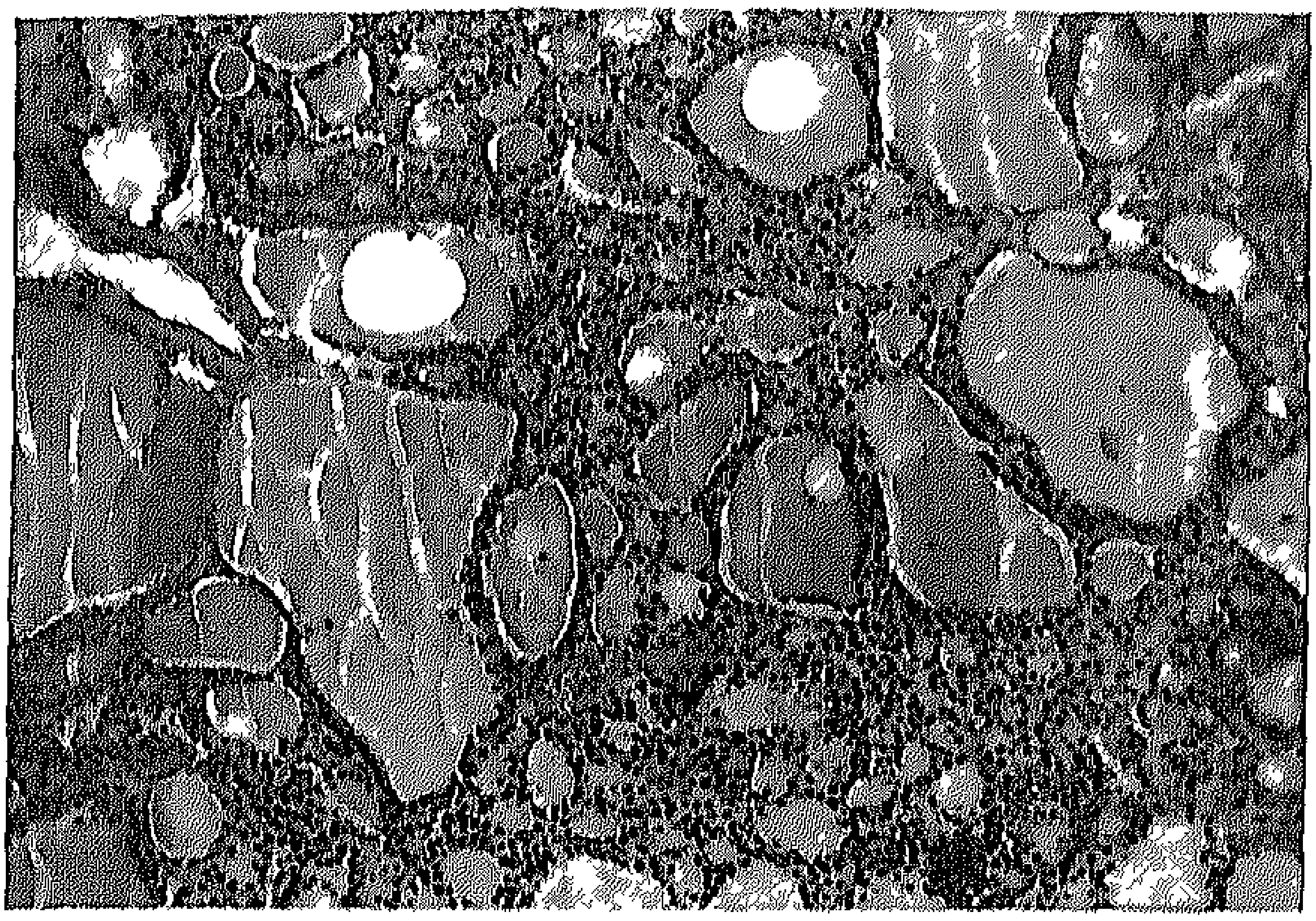


FIG. 193. Thyroid gland showing the follicles containing colloid and interfollicular cell masses. Photomicrograph.

is, they are capable of secreting from either end of the cell, into the follicle or directly into the capillaries by way of the basal end of the cell.

From experimental evidence and observations on cellular constituents such as mitochondria, Golgi apparatus, fat droplets and vacuoles, which are associated with secretory functions of the cells, the general opinion is that the secretion from the follicular epithelium passes from the apex of the cell into the follicle where it is stored until it is needed. Under conditions of excessive stimulation the secretion is thought to pass from the basal portion of the cell directly into the blood stream without passing through a storage phase.

A second type of cell is occasionally found among the follicular cells. These cells are called the *colloid cells of Langendorf* and are characterized by deeply staining, sometimes pycnotic nuclei and a darker cytoplasm which may be filled with colloid. They are undoubtedly degenerating epithelial elements.

The follicles are filled normally with a homogeneous, acidophilic substance, called *colloid,* in which fat droplets, small globules of mucus, detached epithelial cells and a few leucocytes may be present. In sections, the colloid has the appearance of being detached from the follicular wall, a condition due to shrinkage. It may also contain vacuoles, but whether these are spaces originally filled with fluid, or artifacts, is not clear. Colloid is an iodine-containing substance which represents the secretory product of the gland and contains the hormone *thyroxin* held in a loose chemical union.

The follicles function as a storage place for the colloid. By injection of anterior pituitary hormone the follicles can be induced to excrete this stored colloid in a remarkedly short time. The mechanism whereby either the storage or the excretion of colloid is brought about is unknown. Excretion is thought to take place by way of the follicular cells themselves and not through any intercellular channels. It is probable that the colloid which is present in the follicles represents a reserve supply. If the follicular cells secrete the colloid in a greater quantity than is required by the body, the excess is stored in the follicles, under normal circumstances. In cases where production is normal or excessive and storage is absent or minimal a condition of hyperthyroidism occurs.

The interfollicular spaces are occupied by a loose arrangement of collagenous and elastic fibers, the *interstitial connective tissue,* which gives support to numerous blood vessels and lymphatics. The blood vessels end in capillary networks which are closely applied to the walls of the follicles. Small masses of epithelial cells, called *interfollicular cells*, are present in the interstitial connective tissue and represent groups of undifferentiated thyroid cells. They represent rests of fetal

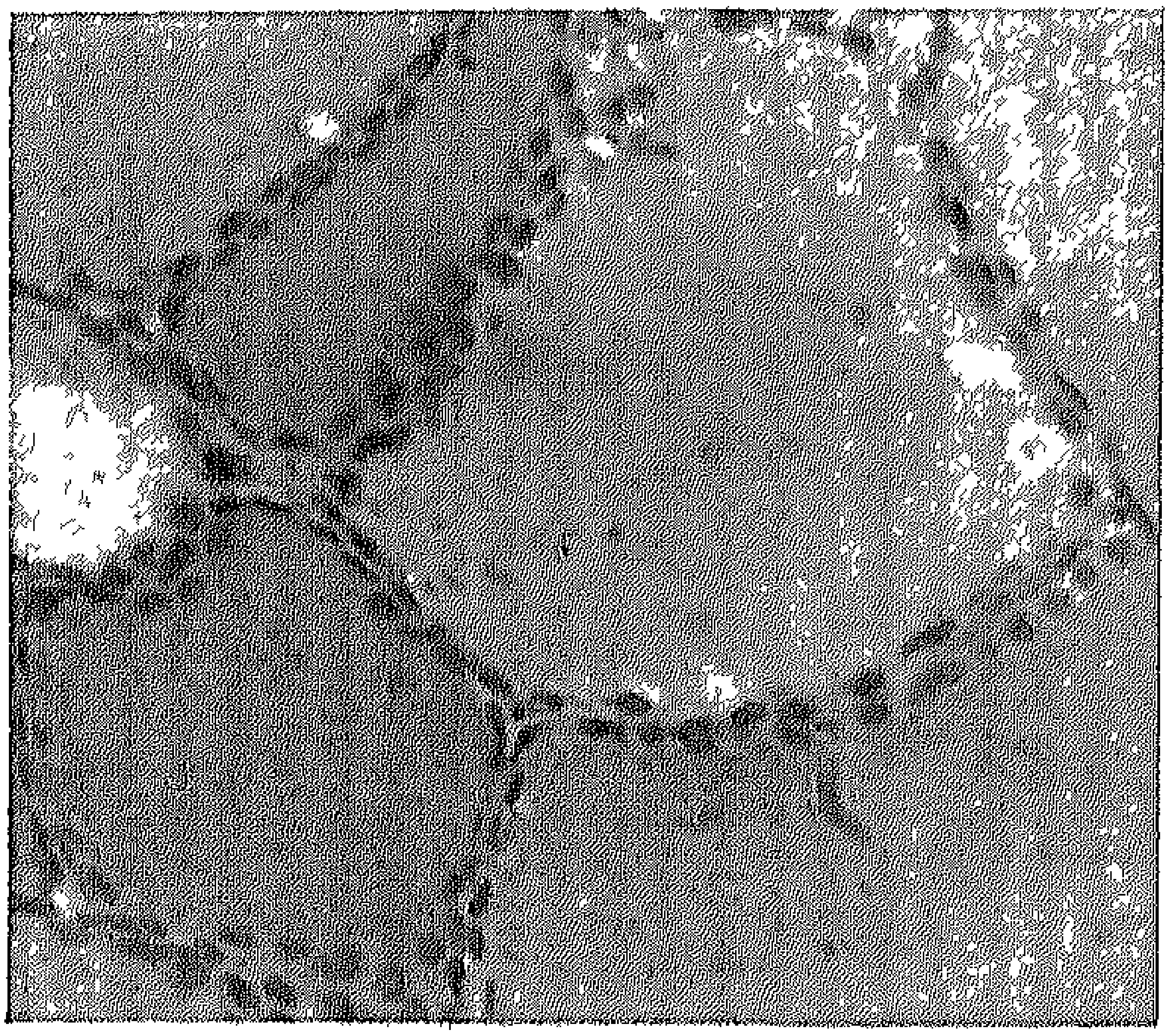


FIG. 194. Section through thyroid showing flattened cells lining follicles, colloid, and several vacuoles at the periphery of the follicle. Photomicrograph.

cells which would normally degenerate. Potentially, they have the capacity, under the proper stimulus, to develop into active thyroid tissue. Small clusters of diffuse lymphocytes occur throughout the interstitial tissue. Under certain abnormal conditions this lymphoid tissue may become hypertrophic and become organized into lymph glands which may encroach on the thyroid tissue to the extent of destroying it.

The thyroid receives its blood supply through branches of the superior and inferior thyroid arteries, which end in dense capillary networks about the follicles.

The lymphatics begin as capillaries about the follicular walls and form lymph vessels, which break up into a series of plexuses in the capsule, the lymph finally passing from the gland to the cervical nodes.

The nerves to the thyroid are unmyelinated post-ganglionic fibers whose cell bodies lie in the cervical ganglia. The cell bodies of the preganglionic fibers are located in the cord at the upper thoracic level. The nerve fibers pass to the walls of the blood vessels and follicles.

In mammals, the thyroid gland will undergo rapid regeneration when only partially removed. However, the degree to which it will regenerate depends on many factors, the most important being the amount of thyroid tissue destroyed and the availability of iodine containing substances. Iodine can retard or prevent regeneration since it must fall below 1.0 mg. per gram before the remaining follicular cells will undergo compensatory activity.

The function of the thyroid gland is the maintenance of a suitable rate of metabolism in the body. This is accomplished by its hormone, thyroxin. Either hypo- or hyper-function of the gland is almost immediately reflected in changes in the physiologic well-being of the individual and in disturbances in other endocrine glands.

THE PARATHYROIDS

The parathyroids are small, reddish, slightly flattened, oval bodies about the size of a pea, which commonly are located on the posterior surfaces of the lateral lobes of the thyroid gland. They usually occur in pairs, a superior and an inferior parathyroid being attached to each lobe. However, this is not constant since two, three, or even four parathyroids may be attached to one lobe, while only one, or none at all, is present on the other. The parathyroids arise from diverticular of the third and fourth pharyngeal pouches.

There is some variation in the manner in which the parathyroids are attached to the lobes of the thyroid, the inferior parathyroids varying more frequently in this respect than the superior. Usually they are more or less completely buried in the substance of the lobe but separated from it by its true capsule. Sometimes, however, they are located on the surface of the lobe under cover of the fascial capsule, but above the true capsule. Occasionally a parathyroid may be attached to the lobe by a slender stalk or peduncle of fibrous tissue, and they have also been found more definitely in relation to the thymus than to the thyroid.

Although closely associated with the thyroid by position, the parathyroids are structurally and functionally separate organs. They are invested by a thin capsule of connective tissue in which a few muscle fibers may be present. Each parathyroid is incompletely divided into lobules by very thin connective tissue septa which extend from the capsule into the gland.

The parenchyma of the parathyroid consists of closely massed epithelioid cells, which are arranged in cords and small masses bordering on thin-walled capillary sinusoids. Two types of epithelioid cells may be recognized: *chief cells*, which are subdivided into chief cells and small dark chief cells, and *oxyphil cells*. These three different cells are not generally regarded as distinct cell types, but rather, as

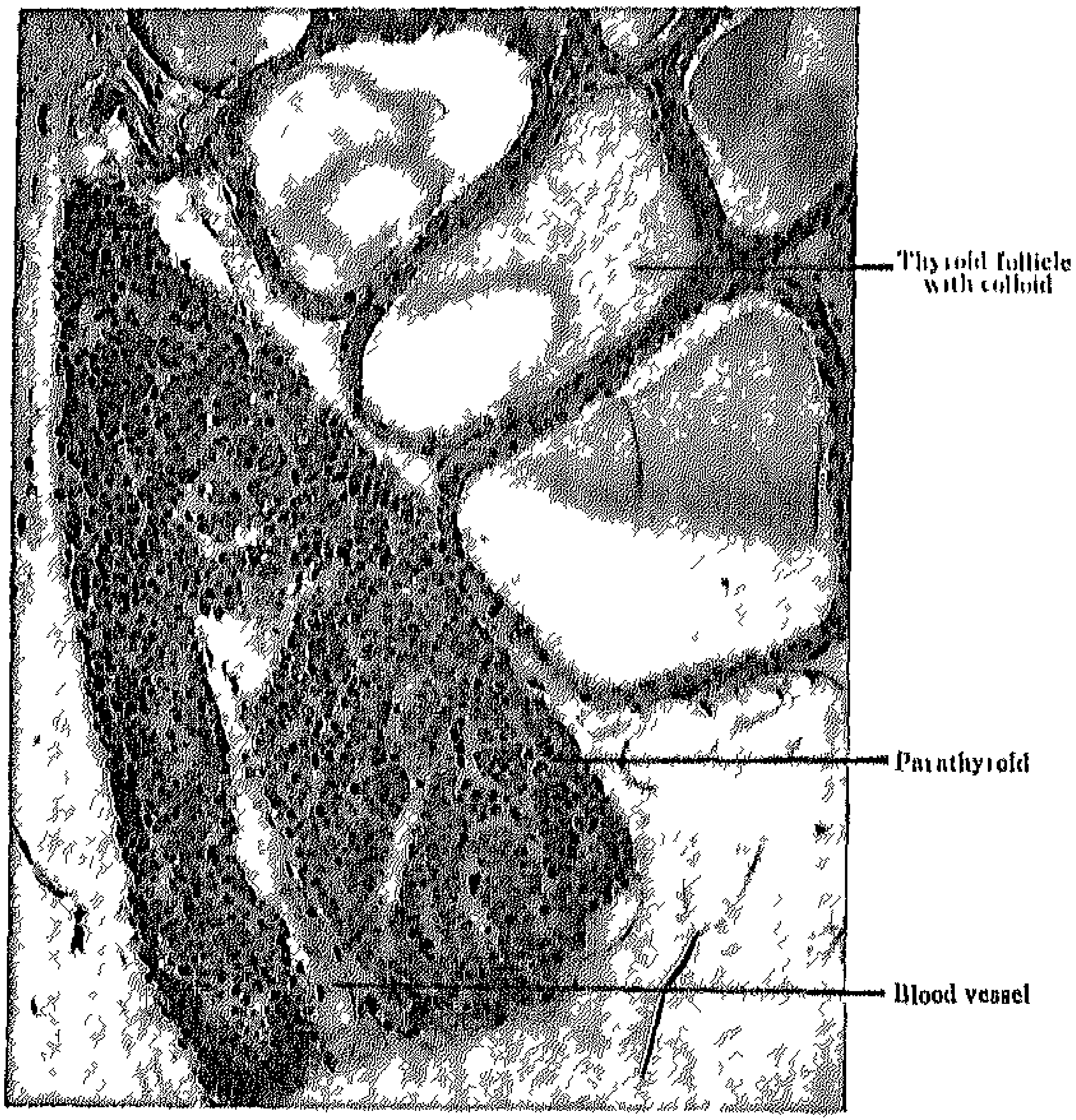


FIG. 195. Thyroid and parathyroid glands. 200 ×. (Courtesy, Snell: "Biology of the Laboratory Mouse," Philadelphia, The Blakiston Company.)

functional stages of the same cell in which the small dark chief cells represent the intermediate form. The chief cells are the most numerous of the cells and up to the eleventh year of life, when the oxyphil cell appears, are the only cells present in the gland.

Chief Cells. These cells are small, polyhedral in shape and have a colorless, clear, nongranular cytoplasm. The nuclei are round or oval, relatively large and vesicular.

Small Dark Chief Cells. These cells appear to be a transitional type between the chief cell and the oxyphil cells. The cytoplasm is filled with faintly staining granules that are extremely fine. The nucleus is smaller and the chromatin more compact than in the chief cells.

Oxyphil Cells. These cells appear in glands at about the eleventh year. They are larger than the chief cells and may occur singly or in masses. They are easily recognized by the large amount of acidophilic, granular cytoplasm they possess. The nuclei are relatively small, round and stain deeply.

All three cells have mitochondria and a Golgi apparatus. The cytoplasm of the chief cells contains more glycogen than is found in the oxyphil cells.

The cell cords and masses lie close to the sinusoids, a condition which provides for the direct transfer of the secretory product of the cells to the blood stream. As age advances, some of the cellular aggregations may develop into follicles in which a small amount of colloid may be present. Unlike that of the thyroid, the colloid of the parathyroids does not contain iodine. The parathyroids differ from the thyroid also, in that they show practically no capacity for regeneration.

The parathyroids receive their blood supply by special branches from the inferior thyroid artery. These branches communicate directly with the sinusoids between the cell cords.

Lymphatics are probably present but are not well understood.

The nerves are unmyelinated fibers which end in the walls of the blood vessels and, probably, in the cell aggregations.

The parathyroid glands are essential for life. Their most important function is the maintenance of the calcium and phosphorus levels of the blood.

THE ADRENAL

The cortex and medulla of the adrenal arise separately in the embryo. The cortex originates in close association with the gonads and their ducts; the medulla being derived from cells which are related to the adjacent sympathetic ganglia. The *chromaffin cells*, which are characteristic of the medulla of the adrenal, are gland cells which are associated with the cells of the sympathetic ganglia in a number of localities in the body where they are known as *paraganglia*. The cortex

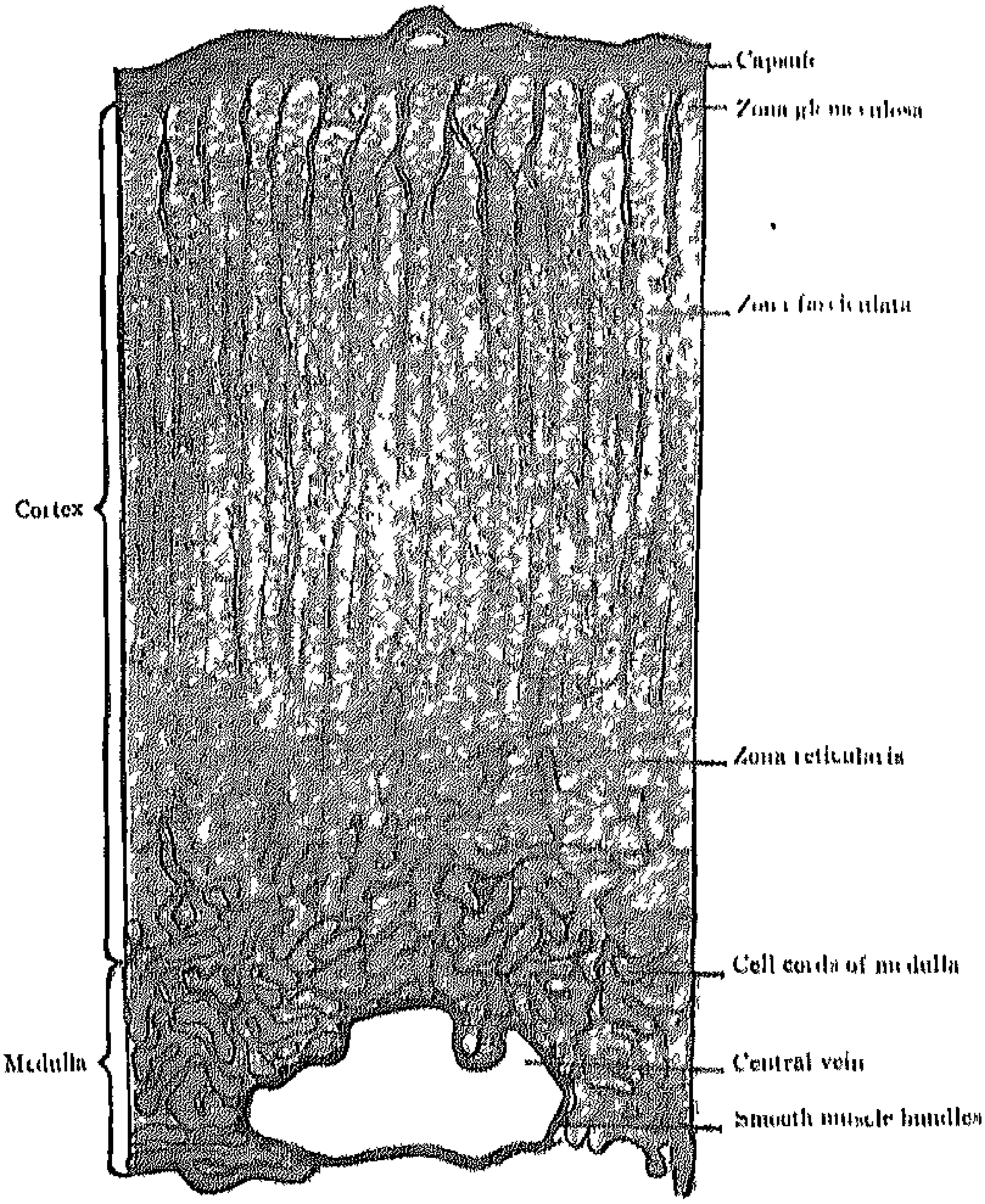


FIG. 196. The adrenal (from sketch by Paul White)

and the medulla are separate structures, which have become so intimately associated in the human adult that they have the appearance of being a single organ. In the lower vertebrates the two parts of the adrenal persist as separate structures throughout life.

The adrenals are small glandular bodies located on the superior poles of the kidneys. Their length varies from 3 to 6 mm.; their breadth being sometimes more, and sometimes less, than half of their length. Their shape has been likened to that of a cocked hat. Although they are closely associated with the kidneys by position, they are neither structurally, nor functionally, related to those organs. Each adrenal consists of two parts, a *cortex* and a *medulla*. In the fresh condition, these areas can be readily recognized when the organ is sectioned, the cortex having a yellowish color due to the presence of fatty substances in its tissues, the medulla having a brownish color on account of the amount of blood which it contains.

The thickness of the medulla varies somewhat in different adrenals. It may be so thin that the reticular area of one side is almost in contact with that of the other, the medullary portion of the gland consisting of a thin sheet of connective tissue in which the central vessels are located.

The cortex is considerably thicker than the medulla and its cells are arranged in cords separated by delicate extensions of connective tissue from the capsule, in which are located the intercolumnar arteries. The cell cords do not rest on a basement membrane but are closely applied to the endothelial walls of the blood vessels which lie between them. The cortex is divided into three zones, according to the arrangement of the cells in the cords: the *zona glomerulosa*, the *zona fasciculata*, and the *zona reticularis*.

The zona glomerulosa is located close to the periphery of the cortex. The cells of this zone are columnar in shape with a pale staining basophilic cytoplasm in which are a few small droplets of fat. Their nuclei are small, deeply staining and round. The cells are arranged in round or ovoid masses, but do not enclose a lumen.

The zona fasciculata consists of cuboidal cells arranged in long, parallel columns. In some areas the cells have a slight radial arrangement. The columns are usually two cells in width. The nuclei are larger and more vesicular than in the glomerular zone, two nuclei occasionally being present in one cell. The cells of the fascicular zone are characterized by large amounts of lipid present in their cytoplasm in the form of small droplets. These droplets are dissolved by the reagents employed in preparing the section for microscopic study, which gives the cytoplasm a spongy appearance, the cells being known as *spongiocytes*. The zona fasciculata comprises the greater part of the cortex.

The zona reticularis is that portion of the cortex which lies nearest to the medulla. It consists of a network of cellular cords formed by the dividing and anastomosing branches of the inner ends of the fascicular columns. The cells which form the cords of the reticular zone vary in appearance, those which are nearest the fascicular zone are lighter in color and contain fat droplets. However, the majority of these cells are filled with pigment, which gives them a dark appearance. Light colored cells containing fat droplets may be seen here and there among the pigmented cells. Between the cords of the reticular zone, the meshes are occupied by thin-walled blood spaces whose endothelial lining is closely applied to the cells of the cords.

The medulla occupies a narrow area between the opposing layers of the cortex. It varies considerably in thickness on account of the difference in the amount of cellular material which it may contain.

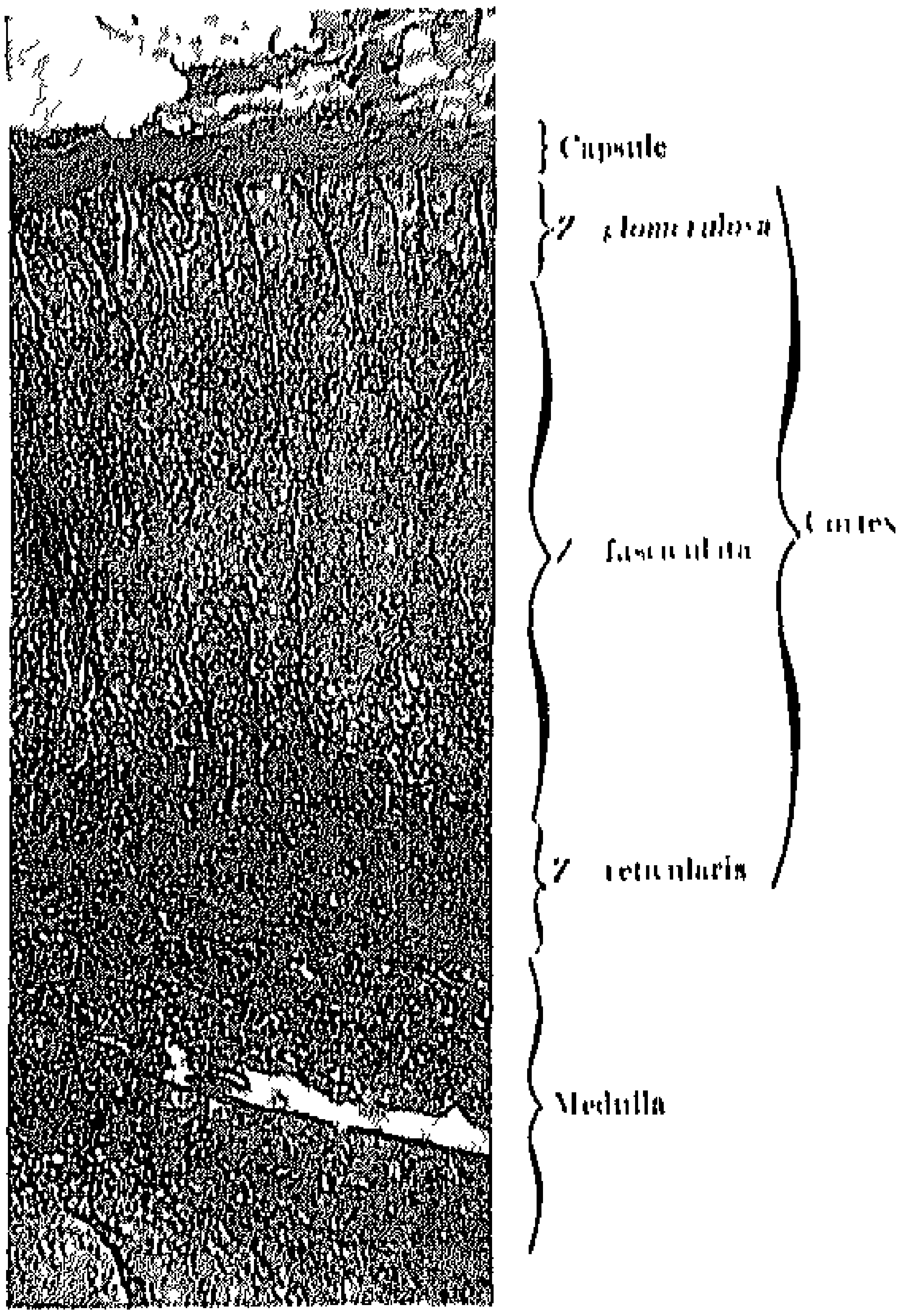


FIG. 197. Section of an adrenal gland (dog). Photomicrograph.

Its cells are arranged in masses and cords which form an irregular network. Owing to the shrinkage which results from the methods employed in the preparation of the section, these cells often assume a stellate form. They are characterized by their large vesicular nuclei and by the presence of fine granules in the cytoplasm which have a characteristic reaction to the salts of chromic acid, which gives the cells a yellowish or brownish color. The medullary cells are called "chromaffin cells" because they show this response.

Blood passes to the adrenals in vessels which pierce their capsules at a number of points. These vessels divide into a number of small branches which extend into the cortex and form capillary networks about the cords. Some of these arteries continue through the cortex to the medulla and end in capillary networks about the medullary cords. The capillaries give rise to veins which unite to form larger vessels which end finally in a large, central vein in the medulla, through which the blood leaves the adrenal.

Lymph vessels arise from capillaries about the zona glomerulosa and also in the medulla. Those of the glomerular area join the lymphatics in the capsule; those which have their origin in the medulla emerge as efferent vessels from the hilum. The lymph drainage is into adjacent lymph nodes.

The nerves to the adrenal are mainly from the autonomic system. They join in forming a plexus in the capsule, from which the fibers follow the arteries between the cords, to end in the walls of the blood vessels and in relation with groups of cells particularly in the zona reticularis. The nerves to the medulla are preganglionic fibers and are distributed in such a manner that one or more end in clawlike terminations around each cell. The medullary cells take the place of ganglion cells and postganglionic fibers, completing a pathway which is quite unique.

Small bodies having a characteristic structure of the adrenal, occur in various parts of the body. They present the structure of the cortex and not of the medulla and are known as *accessory adrenals.* One such body, which occurs constantly in the broad ligament of the uterus, is known as *Marchand's organ.*

Functionally the medullary and cortical portions of the adrenal are separate, as are their origins. The cortex of the adrenal is essential to life, but the medullary tissue can be destroyed and death does not follow.

Numerous steroidal substances have been extracted from the adrenal cortex. These include substances such as corticosterone and desoxycorticosterone, which so far as is known are produced no where else in the body; various substances which display male or female hormone activity; and many other chemicals whose activity and importance is less well understood. Chemically these substances show rather distinct relationships, but their physiological activity may be quite distinct. Corticosterone is importantly involved in certain aspects of carbohydrate metabolism, particularly in the breakdown of protein to form sugar. Desoxycorticosterone, on the other hand, plays an important role in the regulation of salt and water metabolsm. Under abnormal conditions the production of these hormones may be deficient or excessive. In either case disastrous consequences may occur unless steps are taken to correct the aberrant activity. Excessive production of male or female sex hormone by the adrenal may occur in either sex, but the most common expression of such aberrant function is seen in girls or women. In such instances, male sex hormones are produced to an excessive degree and the unfortunate individuals undergo such masculine changes as the development of facial and body hair, loss of scalp hair, deepening of the voice, and increased muscular strength.

The medulla of the adrenal produces the hormone adrenalin. This substance is said to be "sympathomimetic" since it produces the same effects as those which are observed following stimulation of the sympathetic nervous system. In general, it causes contraction of smooth muscle; exceptions are the muscle of the stomach, intestine wall, urinary bladder and bronchioles. Its action on the musculature of the bronchioles causes them to relax, and because of this it is used in the treatment of asthma. It is also effective in the release of glycogen stored in the liver and elevates the rate of metabolic activity. Its effect upon the circulatory system is variable, the blood vessels of the mucous membranes, skin and splanchnic viscera (except the intestinal vessels) showing constriction when physiological amounts are injected while those of the lungs, heart, brain and intestine are dilated. The heart rate and cardiac output are increased in man.

THE PARAGANGLIA

The paraganglia, sometimes referred to as the *organs of Zuckerkandl,* are small structures which arise in relation to the cells of the sympathetic ganglia in various parts of the body. They are also known as the *chromaffin bodies,* because of the characteristic reaction of their cells to the salts of chromic acid (see chromaffin cells, p. 352). Although the chromaffin cells of the paraganglia have the same origin and staining reaction as the cells in the medulla of the adrenal, there is no direct evidence that they secrete the same substance (adrenalin; epinephrine).

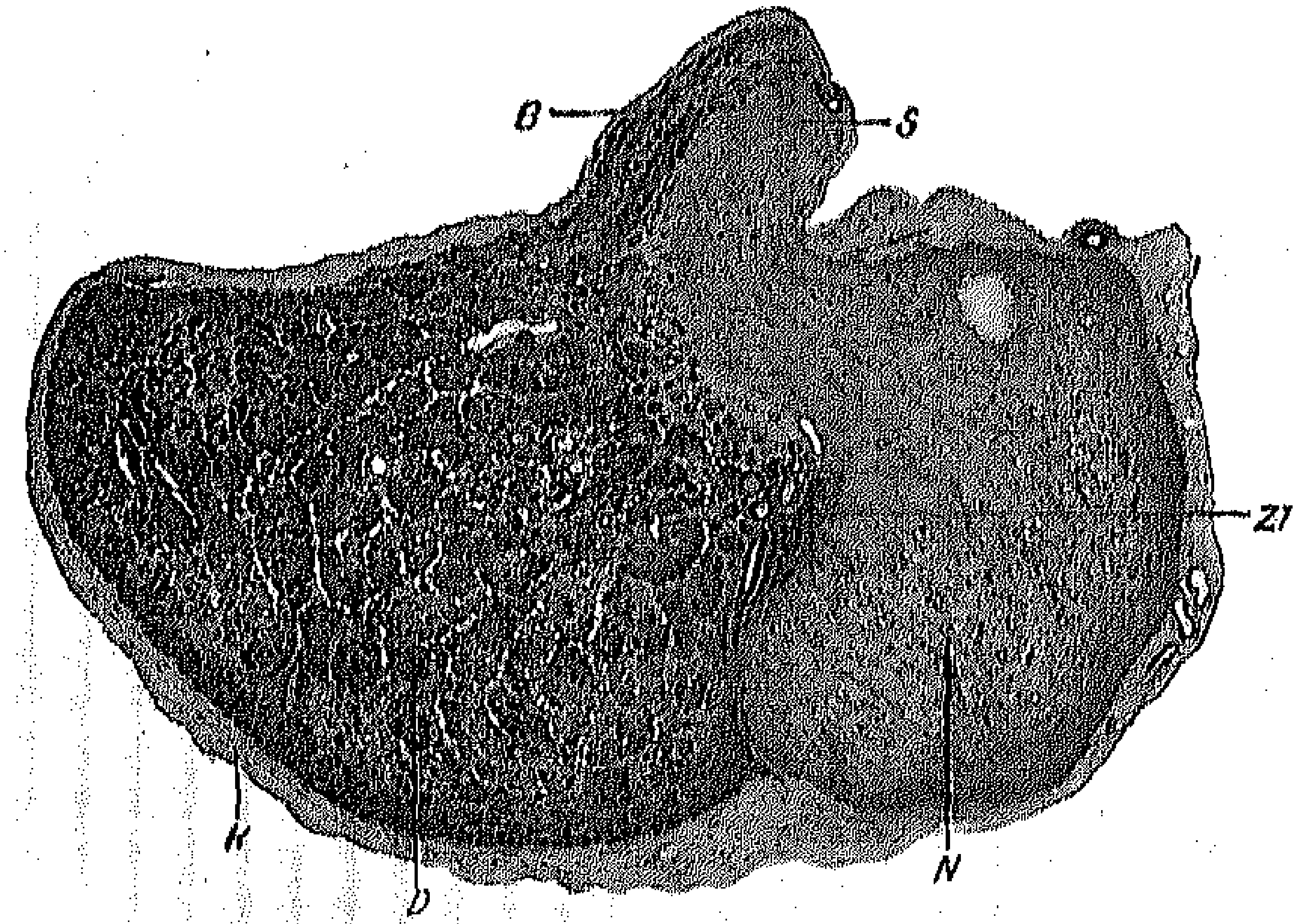


FIG. 198. Median section through the hypophysis of a forty-five year old man. (B) Pars tuberalis. (D) Pars distalis. (K) Capsule. (S) Stalk. (ZI) Pars intermedia. (N) Pars nervosa. (After Schäfer.) (Courtesy, Maximow and Bloom: "Textbook of Histology," Philadelphia, W. B. Saunders Co.)

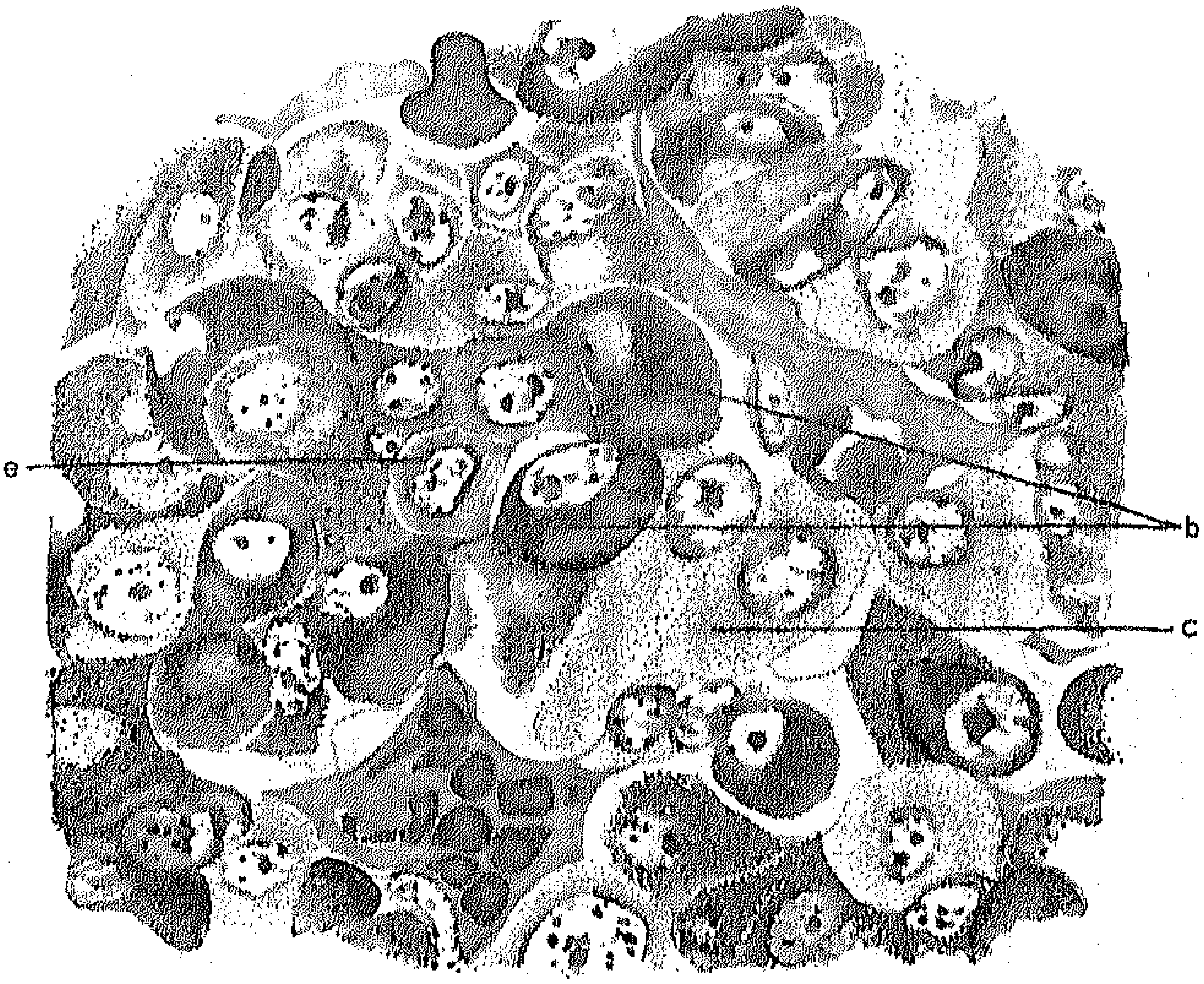


FIG. 199. Pars distalis of the hypophysis of a pig. (e) Alpha cell. (b) Beta cells. (c) Chromophobe cell. (After Maurer and Lewis.) (Courtesy, Maximow and Bloom: "Textbook of Histology," Philadelphia, W. B. Saunders Co.)

THE HYPOPHYSIS

The anterior lobe of the hypophysis is derived from a diverticulum known as *Rathke's pouch* which grows toward the brain from the roof of the oral cavity in the embryo. The posterior lobe is formed by a part of the brain which grows downward from the floor of the third ventricle, just behind the optic chiasma. A portion of the diverticulum from the oral cavity comes into contact with the downgrowth from the brain and becomes the intermediate lobe. The intermediate and anterior lobes are separated during development by a cleft, which is the remnant of the lumen of the diverticulum. In man this cleft usually is obliterated more or less completely. The anterior and intermediate lobes lose their attachment to the oral ectoderm; however, a portion of the primitive stalk may persist as a pharyngeal hypophysis. The downgrowth from the brain is hollow at first, but loses its lumen and becomes solid except for its upper part, into which a portion of the third ventricle projects for a short distance. The lateral portions of the pars distalis (anterior lobe) extend upward and develop into the pars tuberalis, which grows about the stalk and also extends beneath the brain for a little distance.

The hypophysis is a small glandular structure which is attached to the base of the brain by a short stalk, the *infundibulum*. It lies in a saddlelike depression of the sphenoid bone known as the *sella turcica*. The dura mater extends across the sella turcica forming a roof (the diaphragma sellae) and it sends extensions down to ensheath and form the capsule by which the hypophysis is invested. The stalk by which the hypophysis is attached to the brain passes through a small aperture in the diaphragma.

The hypophysis consists of an anterior lobe *(pars distalis)* which forms the principal glandular part of the organ, an intermediate lobe *(pars intermedia)* lying between the anterior and posterior lobes, a posterior lobe *(pars nervosa)*, and a part which envelops the infundibular stalk, the *pars tuberalis*. The size and weight of the hypophysis varies considerably in man, being larger in the female than the male. The weight increases during pregnancy due to an increase in the number and size of the cells of the anterior lobe.

The anterior lobe *(pars distalis)* constitutes the greater part of the hypophysis (approximately 75 per cent). It is composed of cells which are arranged in cords and masses about irregular blood sinusoids. Two main types of cells are present: *chromophils* and *chromophobes*, so called because of their reaction to stains.

The chromophilic cells are characterized by the presence of granules in their cytoplasm and by distinct cell walls. On the basis of the staining reaction of these granules they are subdivided into two groups: *acidophilic cells (alpha cells)* and *basophilic cells (beta cells)*. While there is no clear-cut characteristic distribution of these two cell types in the human hypophysis, there seem to be a few more basophilic cells in the cords around the periphery of the anterior lobe while the central cords contain more acidophilic cells. The chromophobes are scattered throughout both areas tending to occupy the central portions of the cords. The cytoplasm of all three cells contain mitochondria, a Golgi apparatus, and secretion granules. The shape of the Golgi apparatus in the beta cells differs from that of the alpha cells in some animals, but not in man.

The *alpha cells* predominate and show distinct, large, round, acid staining granules in their cytoplasm. These granules are closely packed in the cells and are insoluble in acids and alkalies. They first appear in the hypophysis in fetuses of about three months of age.

The *beta cells* are somewhat larger than the alpha cells. They contain granules which are finer and less distinct than the granules of the alpha cells. These granules appear later in fetal life than alpha granules (end of the third or beginning of the fourth fetal month).

The *chromophobe cells* (also called *chief* or *reserve cells*) are scattered throughout the anterior lobe, but are more numerous in the regions of the pars intermedia and pars tuberalis. They are found in the middle of the columns of cells. The boundaries of the cells are not distinct and they may appear as groups of nuclei that have a common cytoplasmic base. The nuclei are distinct and the cytoplasm is agranular or may occasionally contain only a very few granules.

The relationships of the different cells in the pars distalis have been clarified by recent studies. Although it has been suggested that the alpha and beta cells are not distinct cell types, but are functional aspects of the same cell, this concept has been disproved. Excellent evidence is at hand to show that the alpha and beta cells are independent cell types and have independent secretory cycles. Each evolves through phases of activity during which secretory granules accumulate and are discharged as hormonal substances. It is believed that the cells undergo repeated cycles of granulation and degranulation. During the phase of degranulation the cells are chromophobes. Thus in animals which show different types of Golgi bodies in the alpha and beta cells it is possible to distinguish two types of chromophobes.

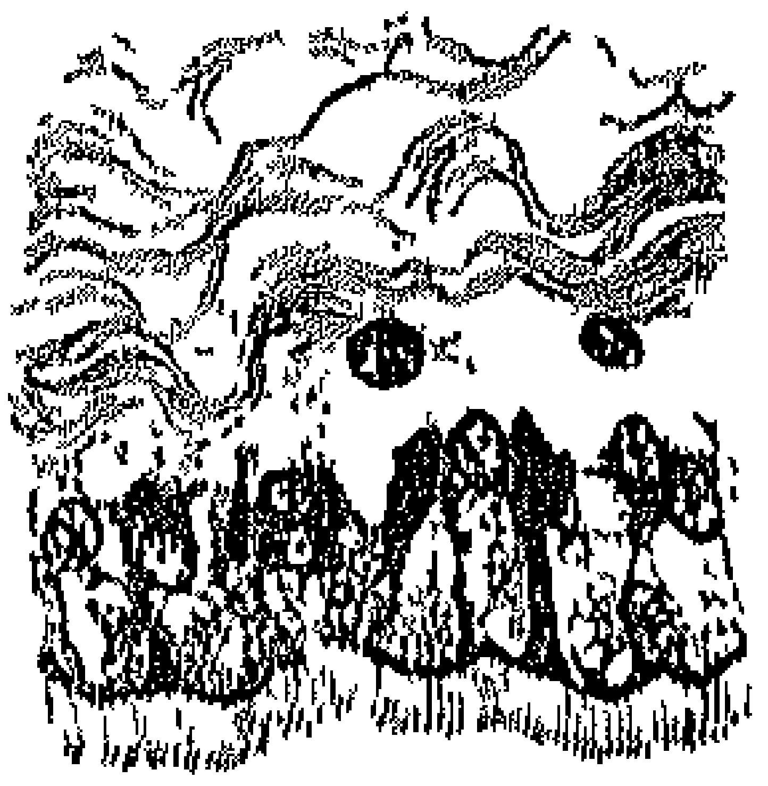


FIG. 200. Ciliated cells of hypophyseal cleft. (Redrawn after Kiyono.) (Courtesy, Cowdry: "Special Cytology," New York, Paul B. Hoeber, Inc.)

While the *pars intermedia* may be recognized in most mammals as epithelial lined spaces containing colloid, located between the pars distalis and the pars nervosa, in the human it is almost indistinguishable. It contains two types of cells: those which react to the basic dyes and which appear to be the more numerous, and those which do not stain readily, being more like the chromophobe cells of the pars distalis. Some of these cells become cuboidal and form follicles in which a substance resembling colloid may be present. In some hypophyses, these basophilic cells may be found migrating into the posterior lobe. The function and fate of these migrating cells is uncertain. Although some people have regarded them as related to hypertensive states, this concept seems to have been adequately denied.

The *pars tuberalis* extends from the anterior lobe to the base of the brain, beneath which it grows about the infundibular stalk. It is said to develop from the lateral lobes of the pars distalis. For the most

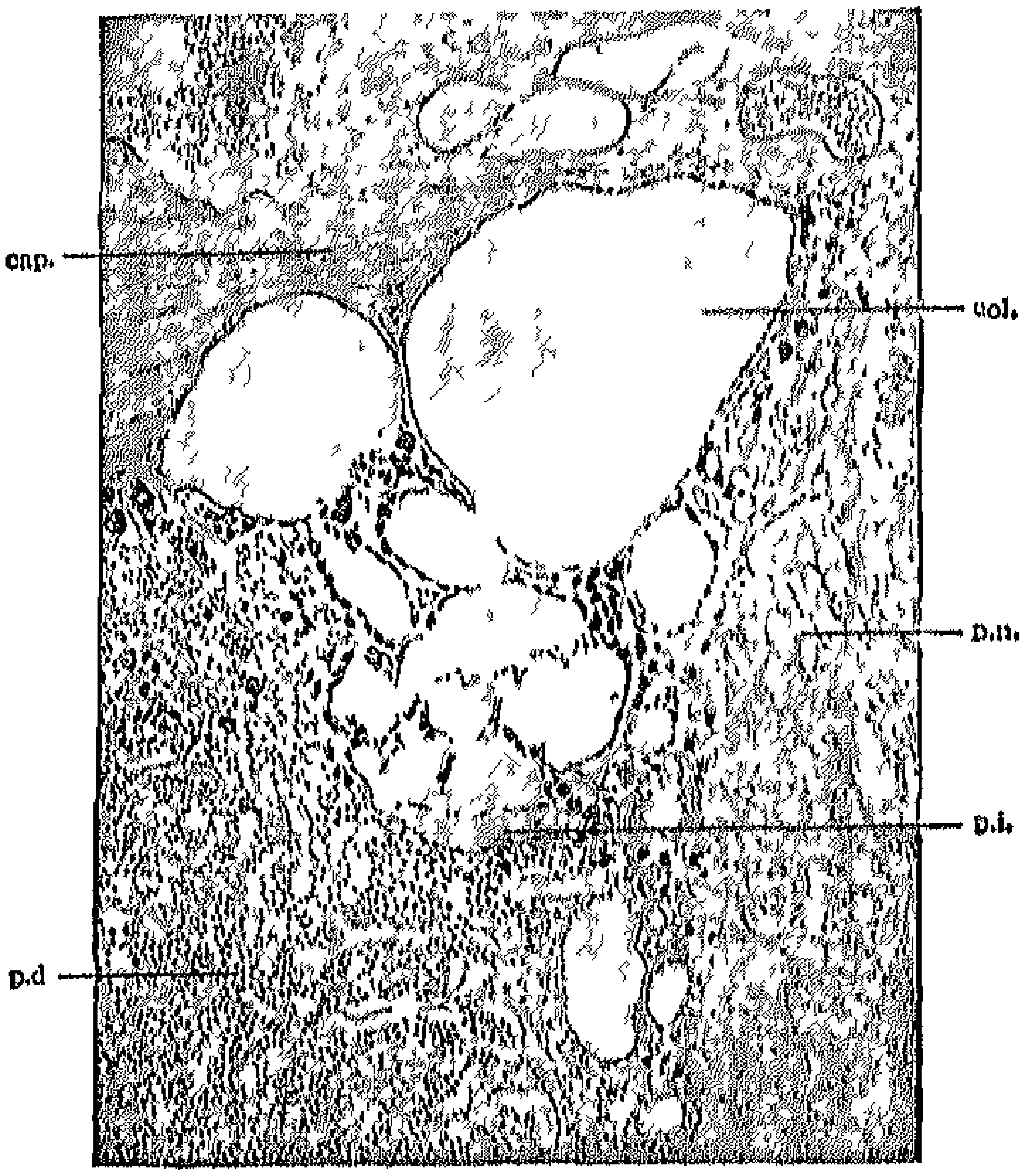


FIG. 201. Junction of glandular and nervous portions of hypophysis (human). (cap.) Capsule (p.d.) Pars distalis. (p.i.) Pars intermedia. (p.n.) Pars nervosa. (col.) Colloid in follicle of pars intermedia (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

part, its cells resemble chromophobe cells in that they do not stain readily; they may also form follicles in which a small amount of colloid is found. Small clusters of squamous epithelial cells are also present and they have been interpreted as representing epithelial rests of buccal ectoderm.

The posterior lobe of the hypophysis *(pars nervosa)* is developed from the floor of the third ventricle, to which it remains attached by the infundibular stalk. It is composed of a form of fibrous tissue which closely resembles neuroglia, and which contains numerous fusiform and stellate cells, known as *pituicytes*. These cells are provided with delicate processes, but are not to be regarded as nerve cells as their form suggests, since they are of ependymal origin and contain no Nissl substance. The pituicytes are characterized by the possession of a brown pigment which gives them a dark appearance. There are no true nerve cells in the posterior lobe of the hypophysis.

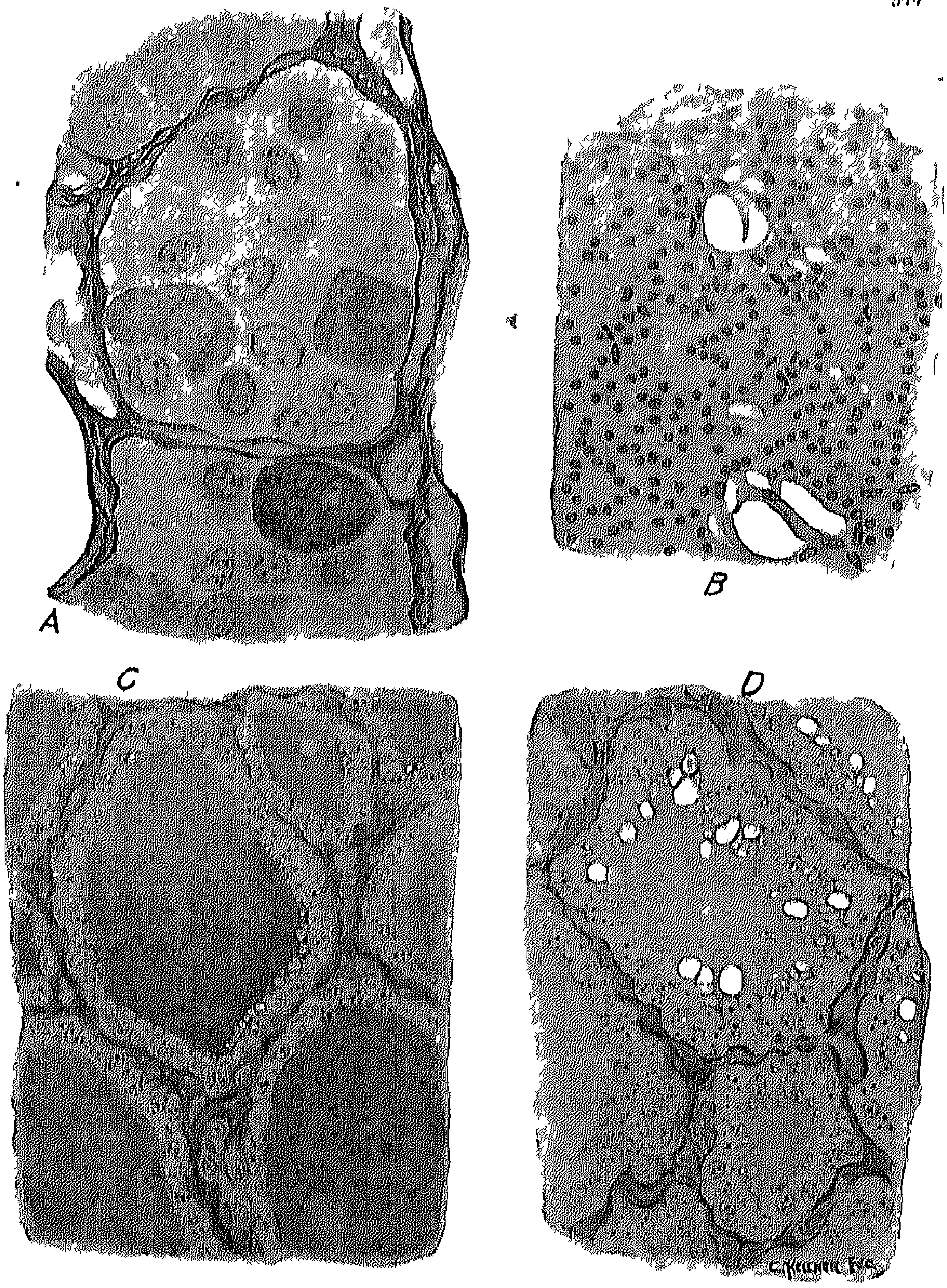


FIG. 202. Anterior hypophysis of executed man. Acidophiles stain pink; three show blue staining Golgi nets. Basophile in lower cord shows a negative picture of a Golgi body as clear canals. Chromophobes are present in middle of central cord. Modified Masson stain. (Courtesy, Smith & Copenhaver. "Bailey's Textbook of Histology," Baltimore, The Williams & Wilkins Co.)

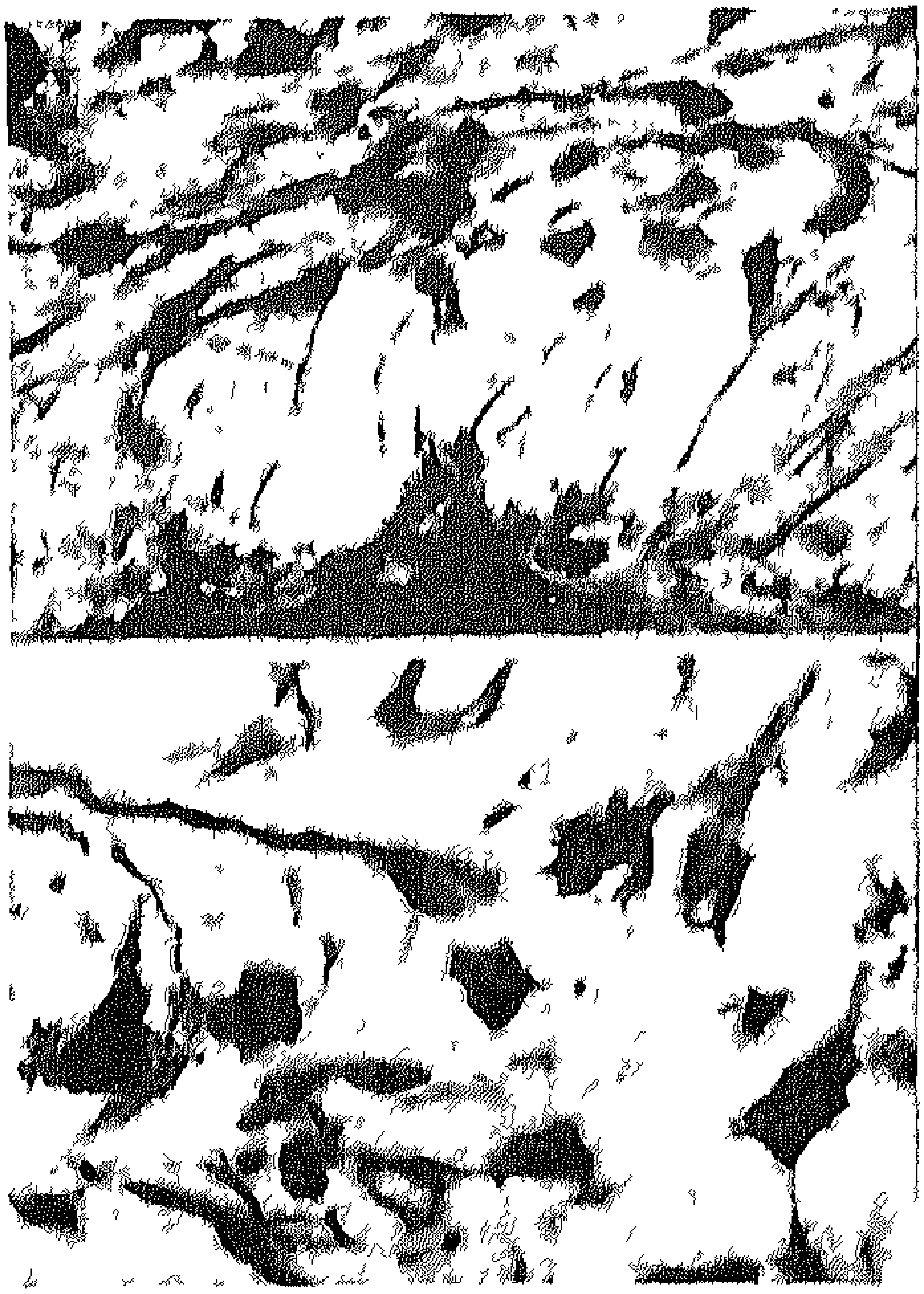


Fig. 203. *(Top)* Pituicytes. Note the many vascular processes radiating to vessel on the right. The cell in upper part of figure similar to an astroblast. Penfield's modification of Hortega's silver carbonate method. *(Bottom)* Cells showing great irregularity in size and shape. Note pigmented cell in lower part of field. (Courtesy, Penfield: "Cytology and Cellular Pathology of the Nervous System," New York, Paul B. Hoeber, Inc.)

The hypophysis has a rich blood supply. Small vessels, the superior hypophyseal arteries, pass from the internal carotids and the circle of Willis to the pars distalis where they join the sinusoids between the cell cords. In addition to this arterial supply, the sinusoids receive venous drainage from the hypothalamus and hypophyseal stalk, according to Wislocki and King. This constitutes a portal system, the significance of which is not certain. The pars tuberalis is supplied by branches from the circle of Willis. The capillaries in the pars nervosa are from the internal carotids by way of the inferior hypophyseal arteries.

The pars intermedia is practically devoid of any vascular supply. The veins from all regions of the hypophysis empty into the cavernous sinus.

The presence of lymphatics has never been demonstrated.

A few unmyelinated fibers which end among the cells of the anterior lobe, arise from the carotid plexus. Abundant unmyelinated fibers, which originate in large part in the supraoptic nuclei of the brain in the region of the optic chiasma, pass down the infundibular stalk and end in the pars nervosa.

Functionally the hypophysis is an extremely complex gland. This gland produces a number of hormones, some of which are closely correlated with the functional activity of other endocrine glands and because of this the hypophysis is often referred to as the "master gland of the body."

The alpha cells of the anterior lobe are thought to secrete a *growth-promoting* hormone which effects the growth and maturation of the skeleton. If the anterior lobe is destroyed at an early age, dwarfism results. If there is a condition of hyperpituitarism in young children, they develop gigantism. However, if this hyperpituitarism occurs in adults they show changes characterized as acromegaly. If the gland is removed in young animals, growth stops, but it can be induced again and maintained by the administration of certain anterior lobe extracts. Nevertheless, the question has been raised as to whether a separate and distinct hormone which controls growth is secreted by the pituitary.

Secretions of this lobe also have a regulatory effect on the function of the thyroid and adrenal glands. The hormone which activates the thyroid gland is known as the *thyrotrophic hormone* and, while it is not definitely known just which cells produce this hormone, it has been suggested that the beta cells are the source of the secretion. This hormone influences the growth of the cells of the thyroid epithelium and it is also related to their secretory activity. The *adrenotrophic hormone* stimulates the cells of the adrenal cortex as indicated by the hypertrophy and the increase in the lipoidal material within the cells of the zona glomerulosa and the zona fasciculata. This hormone also appears to be produced by the alpha cells.

The hypophysis appears to produce three separate *gonadotrophic hormones.* One of these hormones, called follicle stimulating hormone, causes the ovarian follicles to increase in size and stimulates increased production of follicles, while in the male this hormone stimulates the production of the sperm cells. It apparently is produced in the basophilic cells. A second hormone is active in causing the development of the corpus luteum in the ovary in the female and stimulates the interstitial cells in the male. This hormone is commonly called the luteinizing hormone. A third hormone (luteotrophine) stimulates the luteal cells to functional activity. The second and third gonadotrophs are believed to be produced in the acidophilic cells.

The acidophilic cells also produce a substance which is very much like or identical with the last mentioned gonadotrophic hormone. This hormone, known as the *lactogenic hormone*, causes the fully developed mammary gland to secrete milk.

Although claims have been made for the existence of other hor-

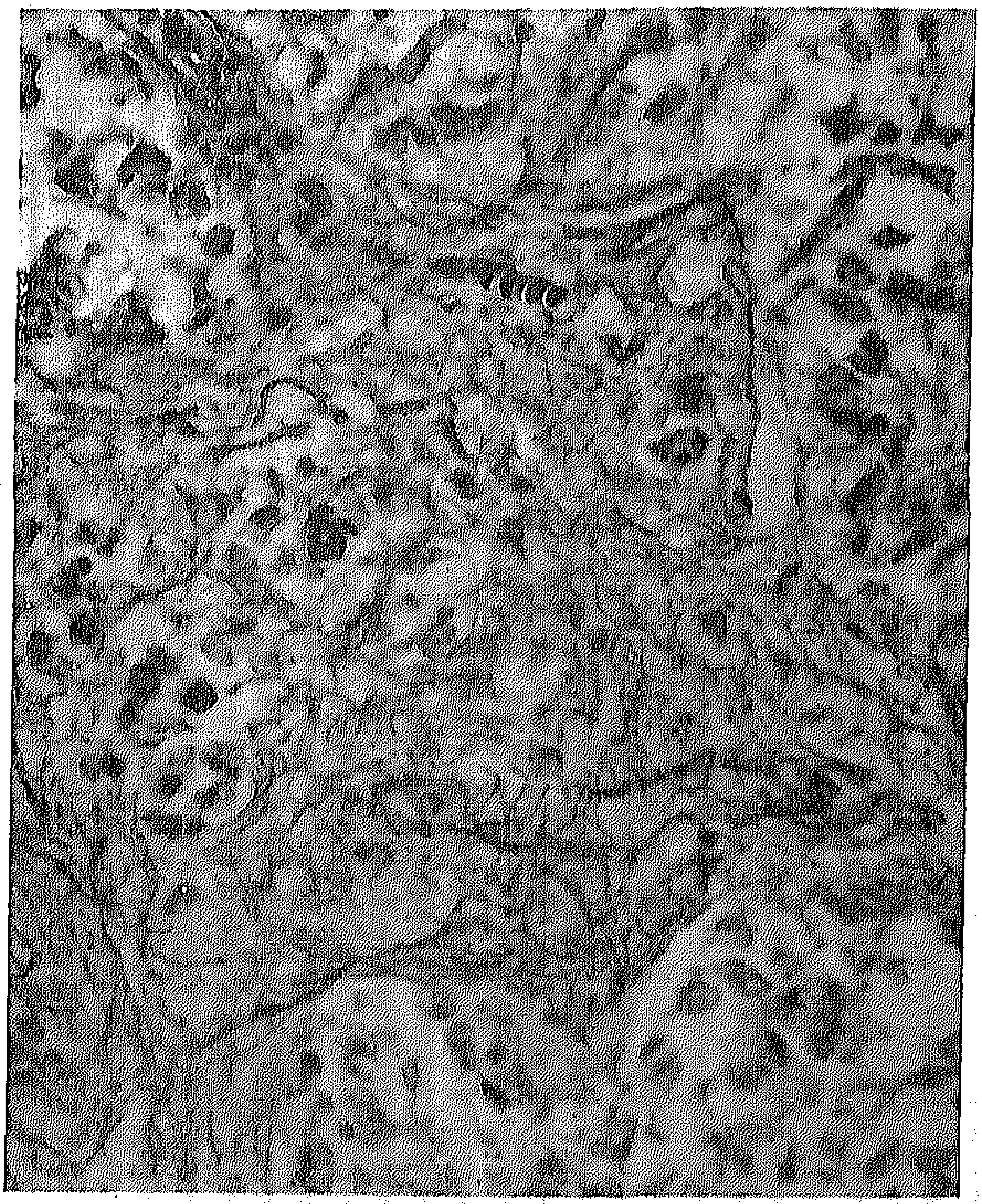


FIG. 204. Human pineal. Bielschowsky. 500 X. (Courtesy, Cowdry: "Special Cytology," New York, Paul B. Hoeber, Inc.)

mones of the anterior lobe, the evidence is not entirely convincing as yet.

Two substances have been isolated from the posterior lobe (pars nervosa): *pitressin*, which has a marked antidiuretic effect and also produces a rise in blood pressure, and *pitocin*, which causes contraction of the smooth muscle of the uterus.

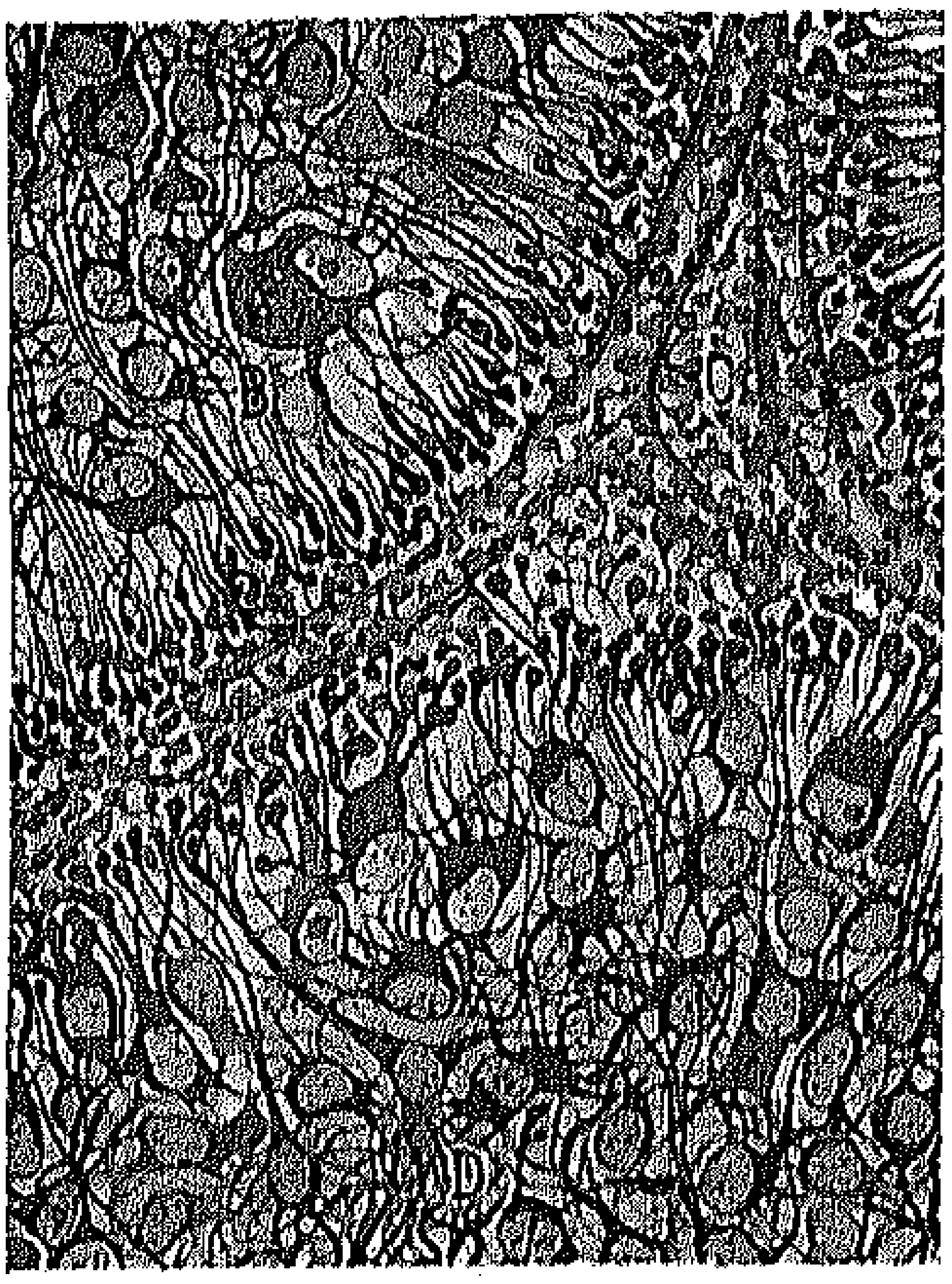
The pars intermedia is believed to produce a substance called *intermedin*. Although this hormone causes an expansion of certain pigment cells in some lower vertebrates its function in man is not known.

THE PINEAL

The pineal or epiphysis is a small, cone-shaped structure, located above the posterior part of the roof of the third ventricle to which it is attached by a narrow stalk. A portion of the ventricle extends into the stalk and is known as the pineal recess. The recess is lined by ependymal cells and is continuous with the ependyma of the ventricle. The capsule by which the pineal is invested is a continuation of the pia mater. Connective tissue septa from the capsule extend into the body and divide its cellular constituents into small, irregular lobes.

Two kinds of cells are found in the pineal body: *neuroglia cells* and *epithelioid cells*. In sections stained with hematoxylin and eosin, the neuroglia cells may be recognized by their small size and deeply staining nuclei. When stained by the silver method, these cells are seen to possess long, branching processes which end in bulblike expansions. These processes form an interlacing network, many of them extending into the connective tissue septa. The epithelioid cells are larger than the neuroglia cells and may contain acidophilic and basophilic granules in their cytoplasm. They are recognized in ordinary preparations, by their pale, vesicular nuclei. Some of the epithelioid cells have a reticulated cytoplasm. This is probably due to fat droplets which have been dissolved out of the cell in making the preparation. It has been claimed by some observers, that nerve cells are present in the pineal body. This, however, has been questioned. In the capsule and connective tissue septa characteristic small, gritty particles called *brain sand (corpora arenacea; acervulus cerebri)* are usually found. These particles consist of calcium carbonate and magnesium phosphate and have a lamellated arrangement. They tend to increase in number as age advances.

The only indication that the pineal body may have an endocrine function is the observation that tumors of the organ may be present when there is early and rapid development of the sexual characters. However, tumors involving adjacent regions of the brain are seen in similar cases and it seems unlikely that the pineal is related in any



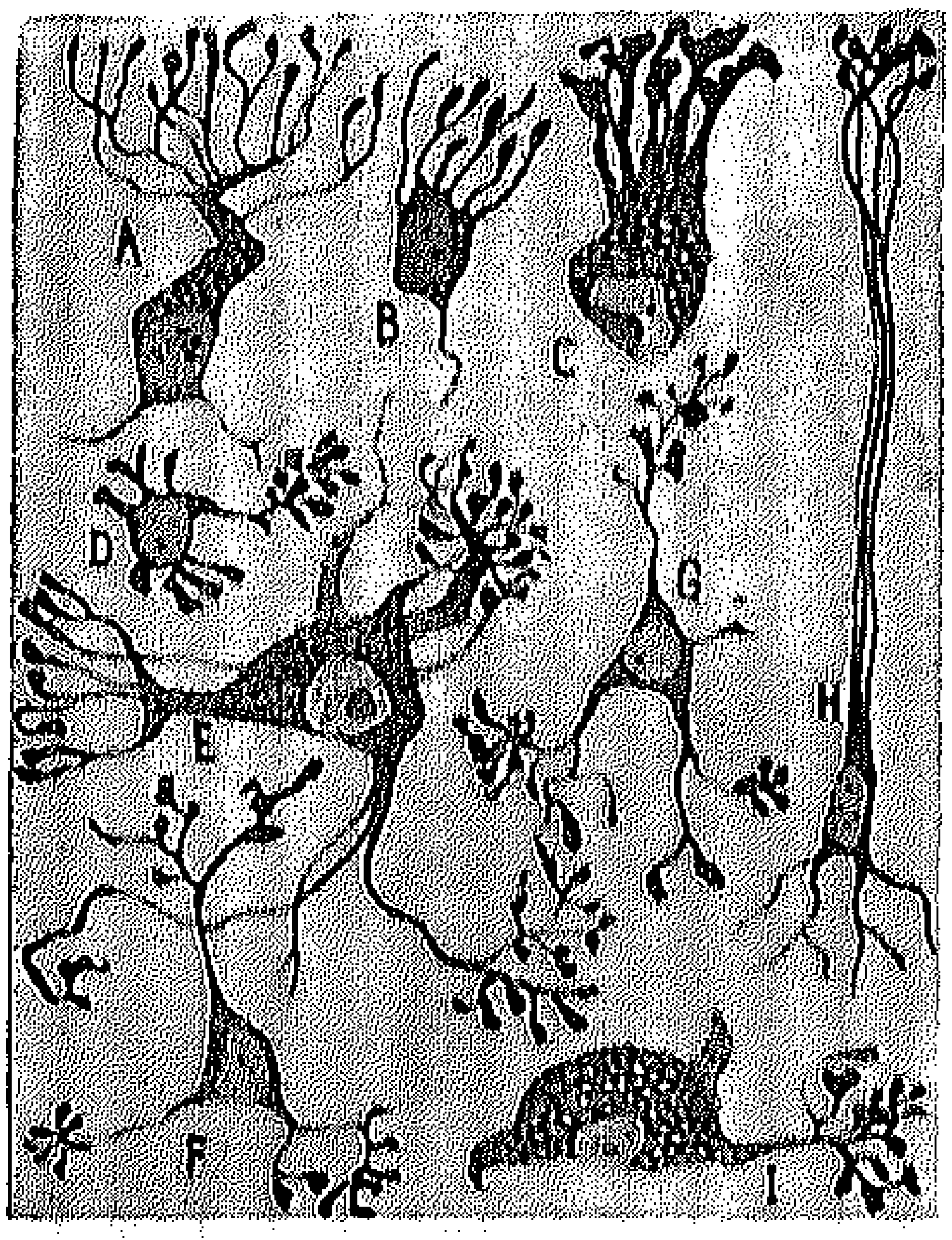


FIG. 205. *(Top)* Semidiagrammatic representation of adult pineal. (A, D) Lobules with polymorphic parenchymatous cells. (B) Neuronoid element. (C) Interlobular space with vessels surrounded by club-shaped prolongations. (Courtesy, Penfield: "Cytology and Cellular Pathology of the Nervous System," New York, Paul B. Hoeber, Inc.)

FIG. 206. *(Bottom)* Parenchymal cells of the adult pineal showing morphological variations. (A, B, C) Cells with prolongations polarized toward the edges of the lobules. (E, F, G) Tri- or multi-polar cells with club-shaped prolongations. (H) Cells with long processes. (Courtesy, Penfield: "Cytology and Cellular Pathology of the Nervous System," New York, Paul B. Hoeber, Inc.)

direct fashion with the sexual precocity. It seems more reasonable to explain these cases in which tumors of the pineal and other structures bordering on the third ventricle are associated with accelerated sexual development on the basis of resultant effects upon the anterior lobe of the hypophysis.

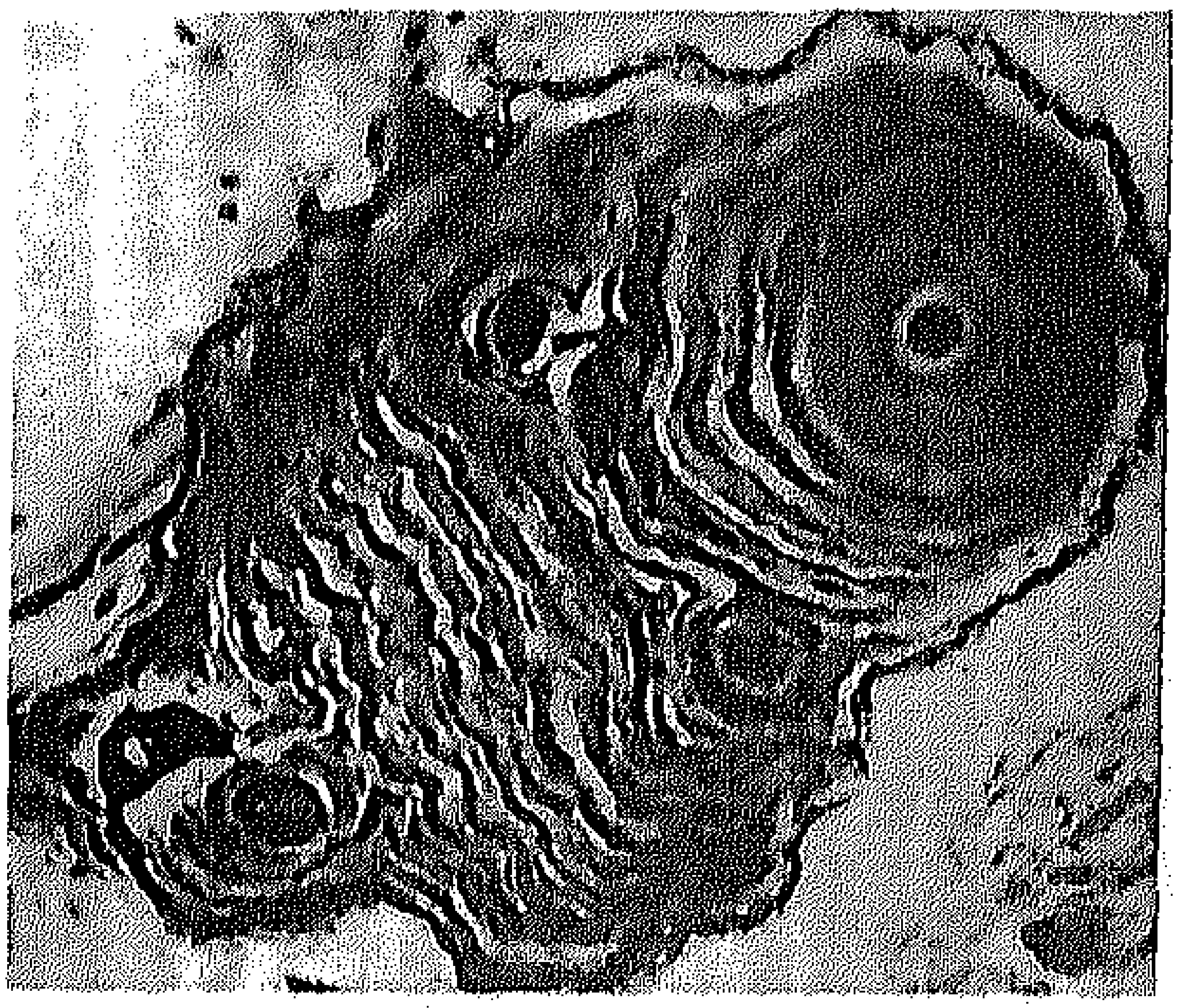


FIG. 207. Acervulus (brain sand) from the pineal of an old person. Note enveloping connective tissue layer. (Courtesy, Penfield: "Cytology and Cellular Pathology of the Nervous System," New York, Paul B. Hoeber, Inc.)

The pineal body has been regarded as a vestigial structure representing the median, or pineal eye of some of the lower vertebrates. Although this possibility has by no means been disposed of, some people have been inclined to regard it as a glandular structure, associated with the median eye. The experimental evidence in support of this, however, is unsatisfactory.

19

The Skin and Its Appendages

The skin is one of the most extensive and important tissues in the body, yet it is usually treated quite lightly. It forms the external covering of the body and as such acts as a guard or barrier between the body and its external environment. In such a position its functions are numerous and varied. Moreover, it gives rise to the hair, nails, and a number of glandular structures spoken of as the appendages of the skin.

One of the most important functions of the skin is to protect the body from harmful substances of its environment. Through the activity of the sweat glands and its vascular supply, it aids in regulating body temperature. It acts as an excretory organ by helping to eliminate water and other waste products. Through the extensive distribution of sensory nerves to the skin, it functions as a receptor for touch, pain, and temperature. The cells of the epidermal layers of the skin are thought to elaborate enzymes (carboxylase, diastase, phenalase, phosphatase and sulfatase). Possibly certain immune bodies are also formed by these cells in response to some of the filtrable viruses.

THE SKIN

The skin consists of two layers: a superficial layer of stratified squamous epithelium called the *epidermis*, and a deep portion, the *derma* or *corium*, consisting of densely compacted fibroelastic tissue derived from the mesoderm. Below the corium is a layer of loose connective tissue in which a considerable, and often variable, amount of adipose tissue is intermingled with loosely arranged connective tissue bundles, the *tela subcutanea*. In cases where the fat is abundant and forms an almost continuous layer, the subcutaneous tissue is called the *panniculus adiposa*.

The skin varies in thickness in different portions of the body. It is quite thin over the eyelids and parts of the external genitalia, moderately thick on the back of the neck and over the shoulders, and is thickest on the palms of the hands and soles of the feet.

The epidermis, sometimes called the *cuticle*, constitutes the outer

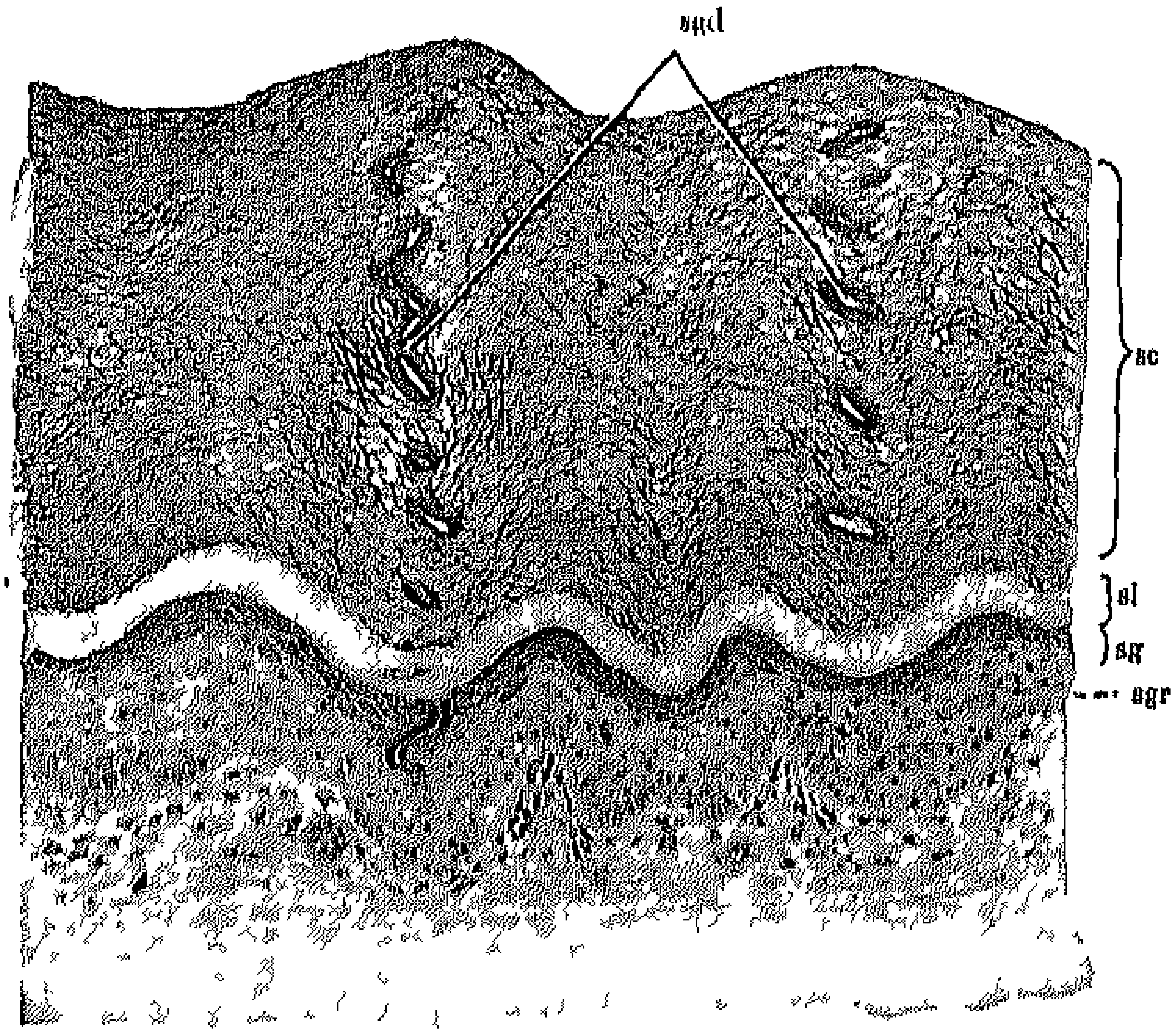


Fig. 208. Skin from the palm of the hand. (sc) Stratum corneum. (sl) Stratum lucidum. (sg) Stratum granulosum. (sgr) Stratum germinativum. (sgd) Ducts of sweat glands.

covering of the skin and in general its thickness varies with the thickness of the skin as a whole. Typically it may be considered as consisting of four rather distinct layers or strata of cells, each of which shows certain definite characteristics. Beginning on the attached surface of the epidermis these layers, in order, are: *stratum germinativum, stratum granulosum, stratum lucidum* and *stratum corneum.* The first two layers are made up of living and vital cells while in the last two layers the cells are either dying or dead. Nowhere else in the body do living and dead cellular elements exist so close together in normal tissue. In areas where the epidermal layer is thin, the stratum granulosum as a layer cannot be recognized and the stratum lucidum seems to be entirely lacking, so that the epidermis appears to be made up of a stratum germinativum and stratum corneum.

The *stratum germinativum* is always present because, as the name implies, it is in this layer where the cells undergo mitosis to replenish and maintain the epithelial layer. This stratum is made up of a number of cell layers, the basal row of which lies on the connective tissue of the corium. The corium is raised into a number of moundlike elevations, the *dermal papillae,* which penetrate the deep surface of the epidermis giving it a papillated or sinuous outline when seen in cross section. The shape of the cells of the stratum germinativum varies considerably.

The basal row consists of a single row of columnar cells (stratum cylindricum). In the next few rows the cells become at first round and and then polyhedral in shape, and in the outer rows of this strata the cells become flattened, their long axes lying parallel to the surface. From the deep surface of the basal row of columnar cells, dentate processes extend into the underlying corium and help to attach the epidermis to the dermis. Except for the basal row of cells, all the remaining cells of this stratum have *intercellular bridges*. These bridges are delicate protoplasmic processes, which extend across the intercellular spaces, passing from one cell to another. When the cells are pulled apart, the processes project from their surfaces giving them a burlike appearance, for which reason they are known as *prickle cells*. The cytoplasm of these cells contains a number of fibers, which can be demonstrated with the use of proper stains. These fibers, known as *tonofibrils*, not only pass through the substance of the cells, but also pass from one cell to another through the protoplasmic bridges, a single

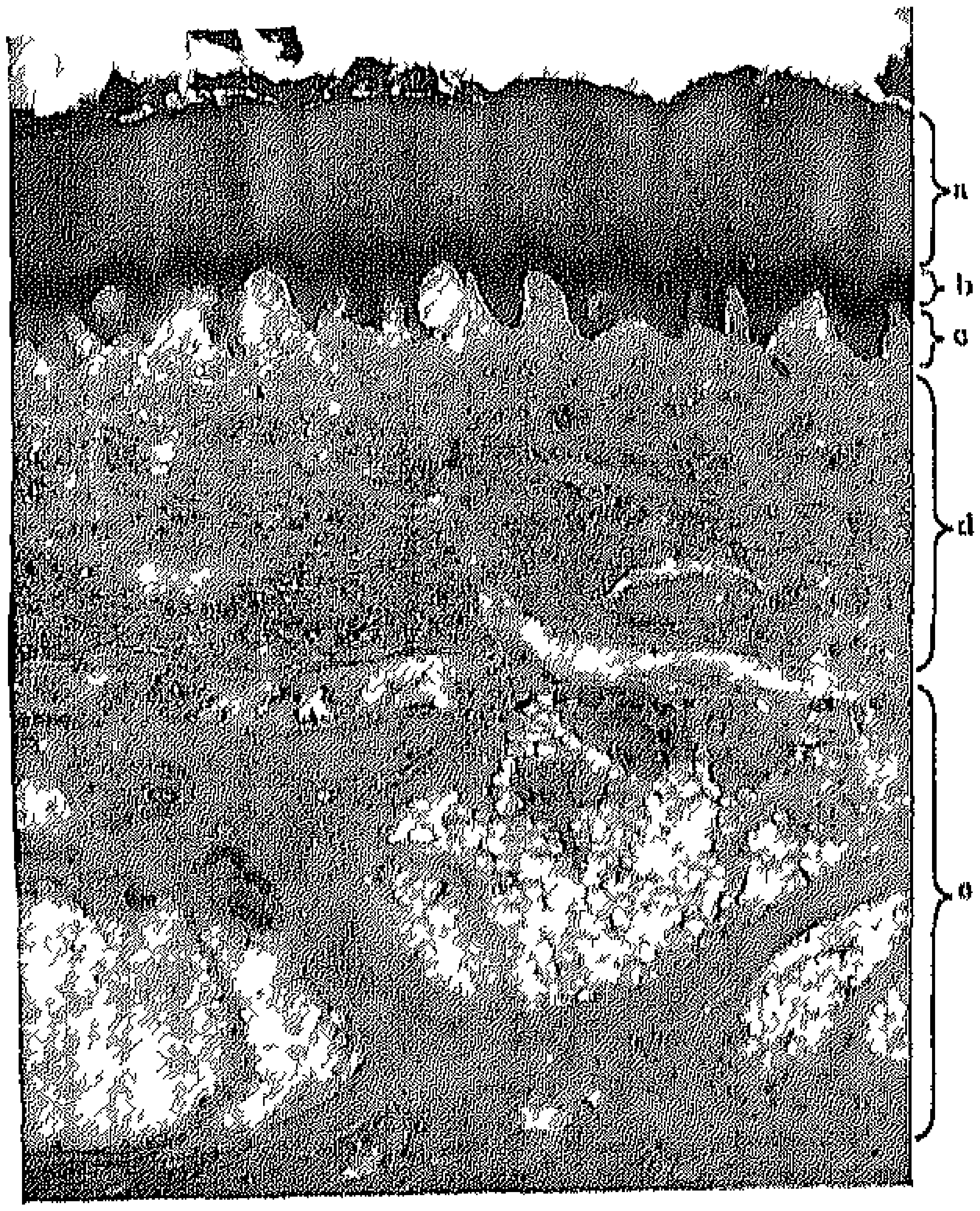


Fig. 209 Skin from the palm of the hand. (a) Stratum corneum. (b) Stratum granulosum (the stratum lucidum is concealed by the depth of the stain) (c) Stratum germinativum. (d) Corium (e) Subcutaneous (loose areolar) connective tissue containing masses of adipose tissue. Photomicrograph

fibril extending in this manner through several cells. These fibrils not only hold the cells in position in relation to one another, but they also give a certain amount of resilience to the tissue. The nuclei are round or oval and stain sharply. As would be expected, there are many cells of the basal row that show mitotic figures. They are not limited, however, to the basal row.

The *stratum granulosum* consists of 1-5 rows of spindle-shaped cells whose long axes lie parallel to the skin surface. The cytoplasm of these cells is filled with deeply staining granules which are the precursors of the substance, *keratohyalin*. The granules are highly refractive and stain intensely with basic dyes and it is thought that the nucleoli and mitochondria may be concerned in their formation. These granules represent the initial stage in the formation of *keratin*, a substance characteristically present in the cells of the stratum corneum. The nuclei of these cells are oval with the long axis of the nucleus parallel to the long axis of the cell. The nuclei are beginning to show characteristics of old age.

The *stratum lucidum* is present only in those portions of the skin where the epidermis has attained a considerable degree of thickness. Ordinarily it appears as a colorless, homogeneous layer due to the refractive properties of the substance, *eleidin*, with which its cells are filled, and which is formed by the liquefaction and coalescence of the keratohyalin granules of the stratum granulosum. Close examination of the stratum lucidum reveals the outlines of its fusiform cells, although it is difficult to distinguish both the cell boundaries and the nuclei.

The *stratum corneum* is only a few cell layers in thickness in certain portions of the body, but is several times that of the rest of the epidermis where the skin is subjected to considerable pressure and attains its greatest thickness. Its cells contain a substance known as *pareleidin*, or *keratin*. The cells of this stratum are at first spindle-shaped, but as they approach the surface they become increasingly flattened and scale-like. The cells of the surface layer are thin, flattened, cornified (keratinized) scales which are removed by desquamation.

The cells of the epidermis contain mitochondria, Golgi apparatus, and intercellular fibrils. In the cells of the stratum germinativum there are many mitochondria present. They decrease in number in the more superficial layers of cells and disappear entirely in the surface layers It has been suggested that these cells give rise to the intracellular fibrils and that they are concerned with the formation of keratohylin and the pigment melanin. The Golgi apparatus can be demonstrated in the germinal layer cells where it is found in the portion of the cytoplasm which is superficial to the nuclei. As we progress toward the surface, the Golgi apparatus fragments, disperses and disappears.

The intracellular fibers are easily demonstrated in the cells of the deepest strata. They are thought to develop from mitochondria and, in turn, when they disintegrate they are concerned with the production of keratohyalin. The water content of the epithelial cells is also greater in the cells of the basal layer and decreases as we progress toward the surface layers. On the other hand, acidity of the cells increases from the basal toward the surface layers.

The epidermis rests on a substratum of connective tissue consisting of two layers: the *corium* and the *tela subcutanea*. No definite boundary exists between these layers, the one merging insensibly into the other.

The *corium (derma)* lies directly beneath the epithelium and consists of a superficial portion, the *papillary layer*, and a deeper portion, the *reticulated layer*. The papillary layer is raised into numerous elevations *(papillae)* which penetrate the deep surface of the epidermis. Between the papillary layer and the epidermis is a thin stratum of reticular tissue in which a few lymphocytes may be found, and which is frequently referred to as the *tunica propria*. The deep, or reticulated, layer of the corium is composed of coarse collagenous fibers, with which a delicate, wide-meshed network of fine elastic fibers is interwoven. The elastic fibers form a more closely meshed network immediately beneath the epidermis.

The *tela subcutanea* lies between the corium and the underlying structures of bone or muscle. In different parts of the body it varies in thickness and in the amount of fat it contains. Its fiber bundles are loosely arranged, the spaces between them being filled with masses of adipose tissue. Beneath the tela subcutanea the connective tissue fibers unite to form a thin, fascial layer, the *fascia subcutanea*.

The color of the skin is modified by the presence of a yellowish brown pigment in the skin. This pigment is usually confined to the cells of the epidermis, but it may also be found in cells of the corium, particularly in the very dark-skinned people. The quantity of the pigment varies in different parts of the body, being especially great in the skin about the nipples, the axilla, in the area around the anus and over portions of the external genitalia. Exposure to ultra-violet light also increases the amount of melanin pigment in the skin, as is readily observed in summer when "tans" are developing.

Melanin occurs in the form of fine intracellular granules in the cells of the stratum germinativum where it may be fairly well restricted to the cells of the basal row (as in white races) or as in the black races, where it may be found in cells throughout the entire stratum and in the deeper cells of the stratum corneum. It is also present in certain specialized cells called *melanoblasts* or *chromatophores*. These are stellate shaped cells located intercellularly in the stratum germinativum. These cells possess fine processes which extend between the epithelial cells of this layer.

In the epithelial cells the melanin is usually found in the more superficial portion of the cell and in this location it is able to give protection to the nucleus against the actinic rays of light which in too great a quantity might be harmful. Both the nucleus and the mitochondria are believed to contribute to the formation of melanin. It has not been definitely proven whether the pigment is formed by the epithelial cells themselves or whether the chromatophores produce it and it then enters the epithelial cells. However, there seems to be good evidence for the belief that it is formed by the epithelial cells themselves. The way the pigment is removed is unknown. That it occurs is well known and in some instances is surprisingly rapid (sudden whitening of hair, etc.). What the mechanism is must still be determined, but it probably lies within the cell itself. Certain other stellate shaped cells *(cells of Langerhans)* are found in the upper layers of the stratum germinativum. They are similar in appearance to the melanoblasts and have been mistaken for them. These cells differ from melanoblasts, however, in some specific stain reactions.

The glands of the skin are the sweat (sudoriferous) and sebaceous glands. The sebaceous glands are closely related to the hair follicles and will be discussed in that connection.

The *sweat glands (glandulae sudoriparae)* are long, unbranched, tubular structures, which end in a series of coils in the deep part of the corium or in the subcutaneous tissue. In passing from the coiled, secreting portion of the gland to the surface of the skin, the duct pursues a straight, or nearly straight, course through the corium. It enters the epidermis between the dermal papillae and after following a winding or spiral course, opens to the surface through a small opening or *pore.* The wall of the duct consists of two or three layers of cuboidal cells which form an epithelium resting on a basement membrane. External to the basement membrane is a thin layer of longitudinally arranged connective tissue fibers. In the epidermis the wall of the duct is formed by the cells between which it passes. The secretory or coiled portion of the gland is somewhat enlarged, its wider lumen being lined by cells that vary in height from cuboidal to columnar. These cells possess deeply staining, spherical nuclei, their cytoplasm being filled with droplets of an oily substance which becomes a watery secretion under the influence of nervous impulses. Between the secretory cells and the basement membrane is a row of elongated, spindle-shaped cells *(myoepithelial cells)* which are, evidently, contractile elements and are regarded as delicate muscle fibers.

The arrangement of the blood vessels in the skin presents a somewhat complicated pattern. The larger vessels penetrate the reticulated layer of the corium, their branches anastomosing to form a network in its deeper portion, the *subcutaneous plexus.* Branches from this plexus pass into the papillary layer, there they unite to form another network beneath the bases of the papillae, the *subpapillary plexus.* Branches from the subcutaneous plexus break up into capillaries in the fat lobules of the subcutaneous tissue and about the secreting portions of the sweat glands. Branches from the subpapillary plexus pass into the papillae, in which they form a series of capillary loops.

The veins which arise from the capillary loops in the papillae unite to form a venous plexus in the papillary layer of the corium. Branches from this network form a second plexus which gives rise to veins that pass to the deep portion of the corium, in which they form a third plexus. This receives most of the venous return from the fat lobules and sweat glands. A fourth venous network is formed in the subcutaneous tissue, from which the larger veins arise that convey the blood from the skin.

The lymphatics are abundant. They originate from capillaries in the papillae and about the sweat glands. These capillaries unite to form vessels which communicate with additional networks of lymph vessels in the corium and in the subcutaneous tissue.

The nerves to the skin are mainly sensory. A few unmyelinated fibers pass to the walls of the blood vessels and to the glands. The myelinated fibers lose their sheaths and end in sense organs, such as Meissner's corpuscles in the papillae, the Pacinian corpuscles in the subcutaneous tissues, and as free endings between the cells of the epidermis.

THE HAIR

The hairs are outgrowths of the skin and are distributed over nearly the entire surface of the body. Hair is not present on the soles of the feet and the palms of the hands. The hairs which occur over the greater part of the body are small, slender and more or less scattered. In areas like the scalp, where they grow more abundantly, the hairs are larger and are set more closely together.

A typical hair consists of a *shaft,* the greater part of which appears above the surface of the skin, and a *root,* which is located in a tubular tructure that lies below the surface of the skin, the lower end of vhich is enlarged and forms the *bulb* of the hair. The bulb is penerated by an upward extension of the connective tissue, the *hair papilla.*

The tubular structure in which the root of the hair is embedded consists of an outer and inner part: the *outer* and *inner* root sheaths. The outer sheath is formed by an invagination of the epidermis, while

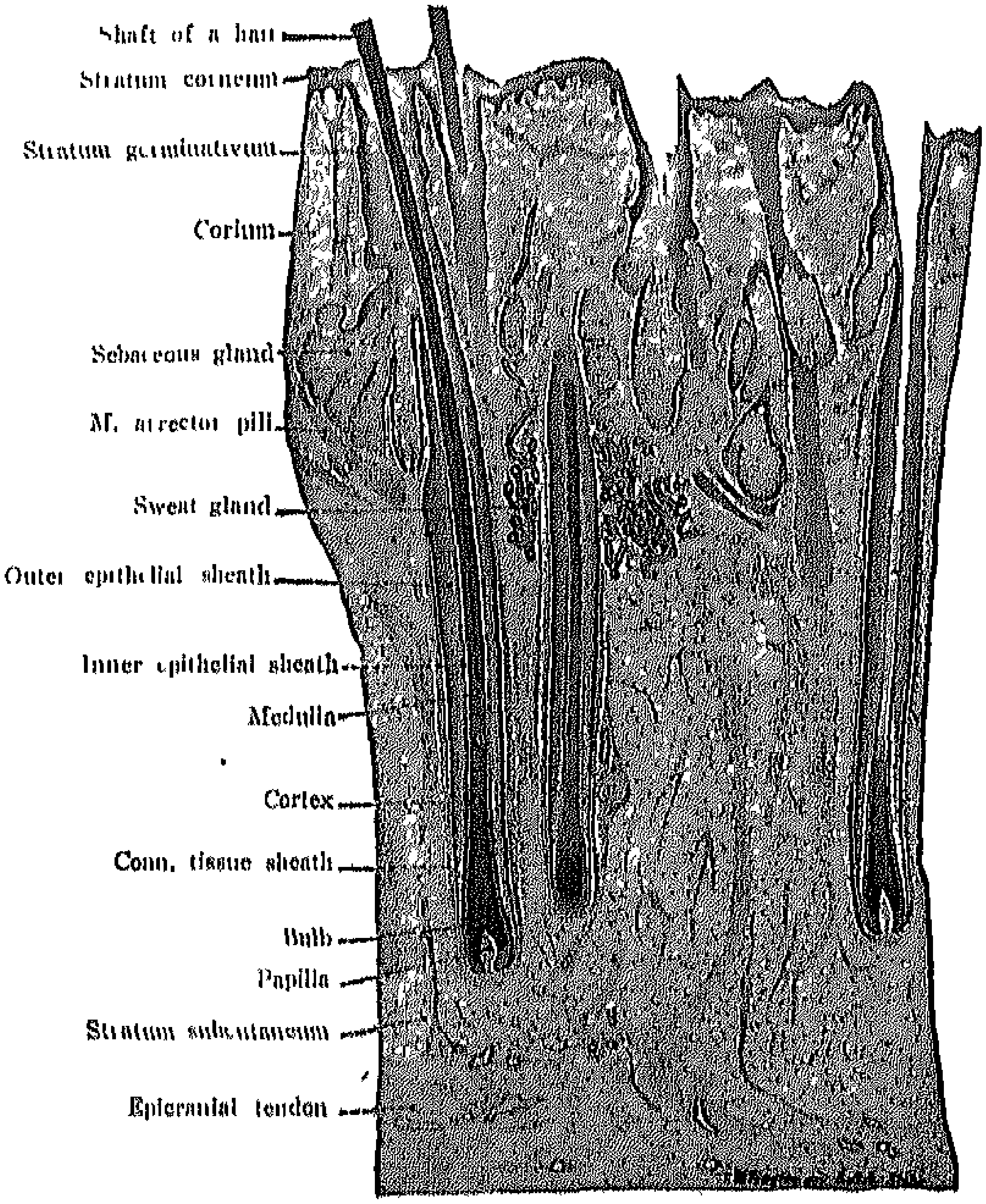


FIG. 210. Thick section of the human scalp. 20 X. (Courtesy, Bremer-Weatherford: "Text book of Histology," Philadelphia, The Blakiston Company.)

the inner sheath is derived from the cells of the outer sheath. The root sheath and the portion of the hair below the surface of the cuticle constitute the *hair follicle*. Surrounding the follicle, in all but the smallest and most delicate hairs, is a connective tissue investment called the *theca*.

As it lies in the skin, a hair follicle is directed obliquely so that an upper and lower surface may be ascribed to it. This oblique direction also results in the hair emerging from the epidermis at an angle. The opening through which the hair passes to appear on the surface is called the *mouth* of the follicle, while the constricted portion of the follicle below the mouth is known as the *neck*. The sebaceous glands which open into the neck of the follicle are usually located in relation to its lower surface, however, in some cases the follicle may be com-

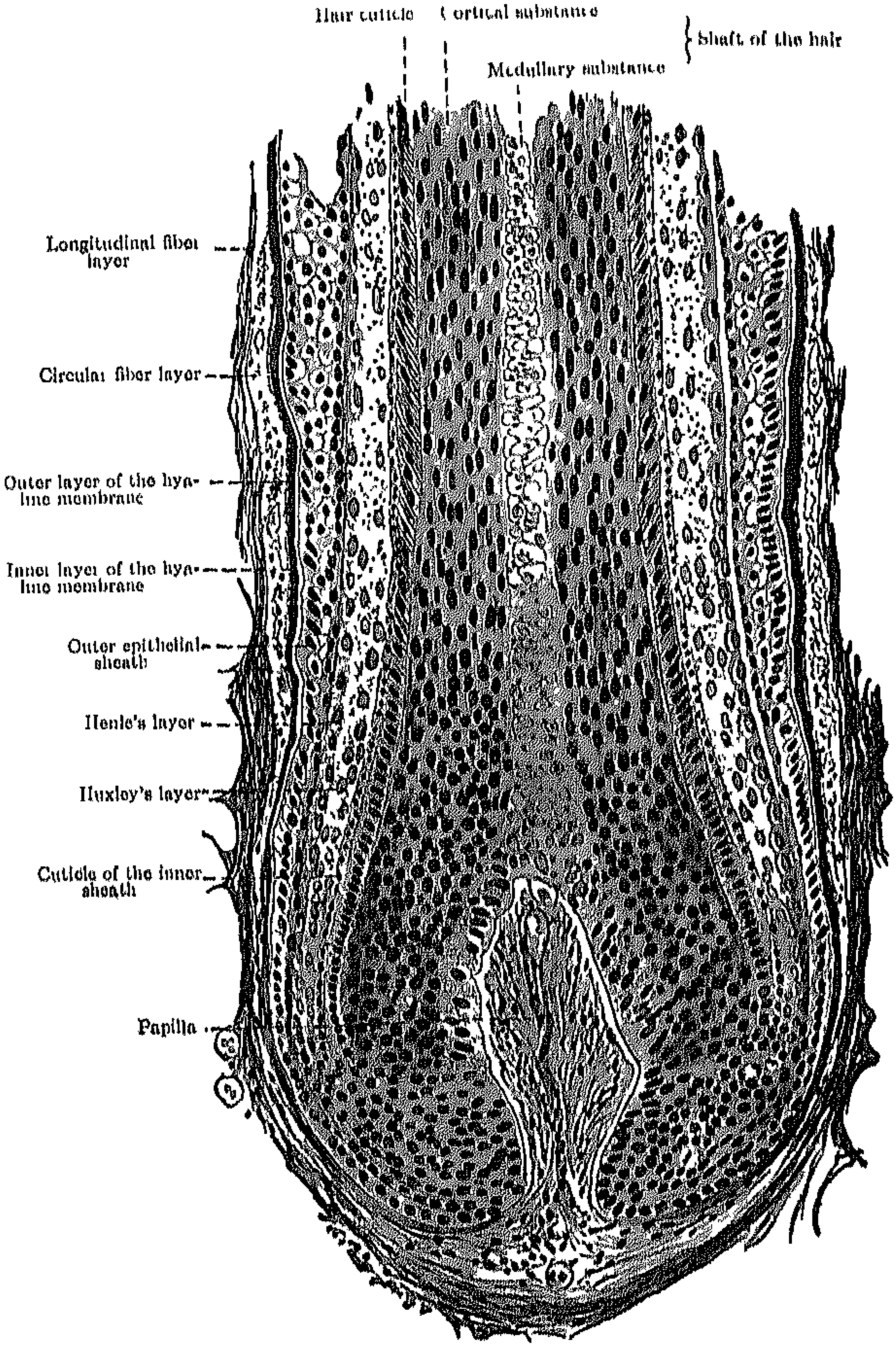


FIG. 211. Longitudinal section of the lowest part of the root of a hair. From a section of the human scalp. 200 ×. The keratohyalin granules are colored red. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

pletely surrounded by these glands. Small, flat bundles of smooth muscle fibers, known as the *arrectores pilorum muscles*, have their origin in the upper part of the corium and, passing obliquely downward, are inserted into the lower side of the follicle below the attachment of the glands. When these muscles contract, the follicles and the contained hairs are elevated. The muscles are arranged about the sebaceous glands in such a way that when they contract, they press on the gland and thus aid in forcing its secretion into the follicle.

The theca or connective tissue by which the follicle is invested consists of an outer layer of loosely arranged, longitudinal fibers, among which are a few elastic fibers. It is also richly supplied with blood vessels and nerves. The middle layer is somewhat thicker and consists of circularly arranged connective tissue fibers. The inner layer, which is thin and has a homogeneous, glassy appearance, is known as the *hyalin membrane*. It forms a basement membrane on which the epithelial cells of the outer root sheath rest and can be traced the entire length of the follicle. It becomes quite thin as it passes around and over the follicle.

The outer root sheath is a continuation of the stratum germinativum of the epidermis. The basal row of cells (corresponding to the stratum cylindricum) are columnar. Internal to the row of columnar cells, the outer root sheath consists of several layers of polyhedral cells, between which protoplasmic bridges can frequently be seen. As this layer approaches the bulb, the inner cells lose their characteristic arrangement; the basal cells forming a single row of cuboidal cells which become columnar as they are carried over the papillae

The inner root sheath, although occupying a position in relation to the outer root sheath corresponding to that of the stratum granulosum, is not a continuation of the granular layer. It occupies the lower two-thirds of the follicle and does not extend above the point where the ducts of the sebaceous glands open into the neck. Its best development is to be observed in the middle third of the follicle.

The stratum corneum extends into the follicle as far as the openings of the ducts of the sebaceous glands. Neither the stratum granulosum nor the stratum corneum continues below the neck of the follicle. The stratum granulosum may continue as far as the extent of the stratum corneum or it may extend slightly below it

The inner root sheath consists of three layers: the outer, known as *Henle's layer*, is a single row of flattened, cornified cells in which the nuclei are indistinct. The middle, or *Huxley's layer*, is composed of one to three rows of cuboidal cells in which the nuclei are more distinct. The inner or *cuticular layer* consists of flattened non-nucleated, cornified cells arranged so that they overlap one another after the fashion of shingles on a roof, the free borders of the cells being directed downward.

The layers of the outer and inner root sheaths become indistinct at the lower end of the follicle and finally merge into an undifferentiated mass of epithelial cells called the *matrix*. This mass of undifferentiated cells forms the portion of the bulb which lies on and about the papilla. The number of cells in the matrix is increased by proliferation from the cuboidal cells which continue the basal layer of the outer root sheath around the bulb. As new cells are formed, the older cells are pushed upward and are differentiated into the cellular elements of the hair.

In the larger hairs, the hair shaft includes a *hair cuticle*, a *cortex* and a *medulla*. The hair cuticle consists of a layer of scalelike cells which overlap, their free edges being directed upward. This enables them to engage the scalelike cells of the cuticle of the inner root sheath in such a way that the dead portions of the sheath are carried out of the follicle by the growth of the hair shaft. The cortex constitutes the greater portion of the shaft. The cells of the matrix are differentiated into long, spindle-shaped elements with rodlike nuclei. These elongated cells, or *hair spindles*, are pushed upward into the shaft as new cells are formed beneath them. They are so closely packed together that it is difficult to distinguish them as separate structures in ordinary preparations. The color of the hair depends on the amount and depth of color of the pigment which these cells contain. Minute clefts or air spaces are present between the cells and have a modifying effect on the color of the hair. Pigment granules are said to be present in these spaces. The medulla consists of two or more rows of cuboidal cells in which there are evidences of degeneration. It is not present in the smaller hairs and is frequently absent from those of larger size. When present, it does not extend the entire length of the shaft and may be interrupted frequently.

Associated with the hair follicles are large, branched saccular glands, the *sebaceous glands (glandulae sebaceae)*, two or more of which may open by their ducts into a single follicle. These glands are epithelial outgrowths from the outer root sheaths, the epithelium of the duct consisting of two or three rows of cells, which are reduced to a single row that encloses the saclike extensions of the gland. The large, rounded cells with which the body of the gland is filled are derived from this basal layer by division. The cells occupying the body of the gland develop fat droplets which are transformed into the oily secretion of the gland *(sebum)*. As the cells in the region of the duct disintegrate and pass into the duct, the secretion is released. It serves for the softening and protection of the hair and scalp.

There is a periodical shedding and replacement of the hair in many of the lower animals. In man this is a more or less constant process. The cells of the bulb cease to proliferate and begin to cornify. The

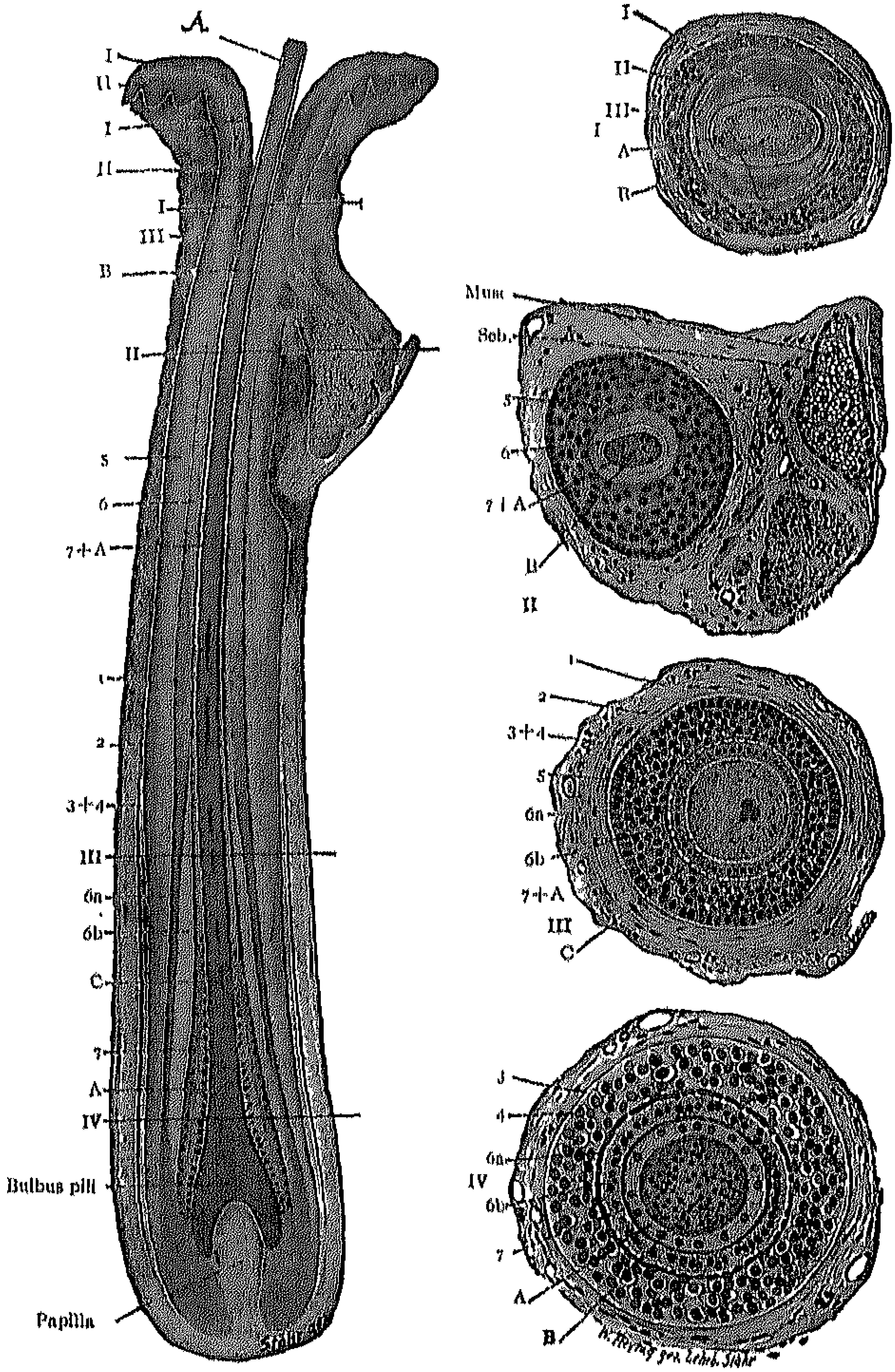


FIG. 212. Four cross sections of a hair of the head (100 ×), with a diagrammatic longitudinal view for orientation. (A) Cuticula. (B) Cortex. (C) Medulla. (I) St. corneum. (II) St. germinativum. (III) Corium. (1-3) Connective tissue sheath. (1) Longitudinal fiber layer. (2) Circular fiber layer. (3) Connective tissue hyaline membrane. (4) Epithelial hyaline membrane. (5) Outer epithelial sheath. (6) Inner epithelial sheath. (6a) Henle's layer. (6b) Huxley's layer. (7) Cuticula of the sheath. (Musc.) Arrector pili. (Seb.) Sebaceous gland. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

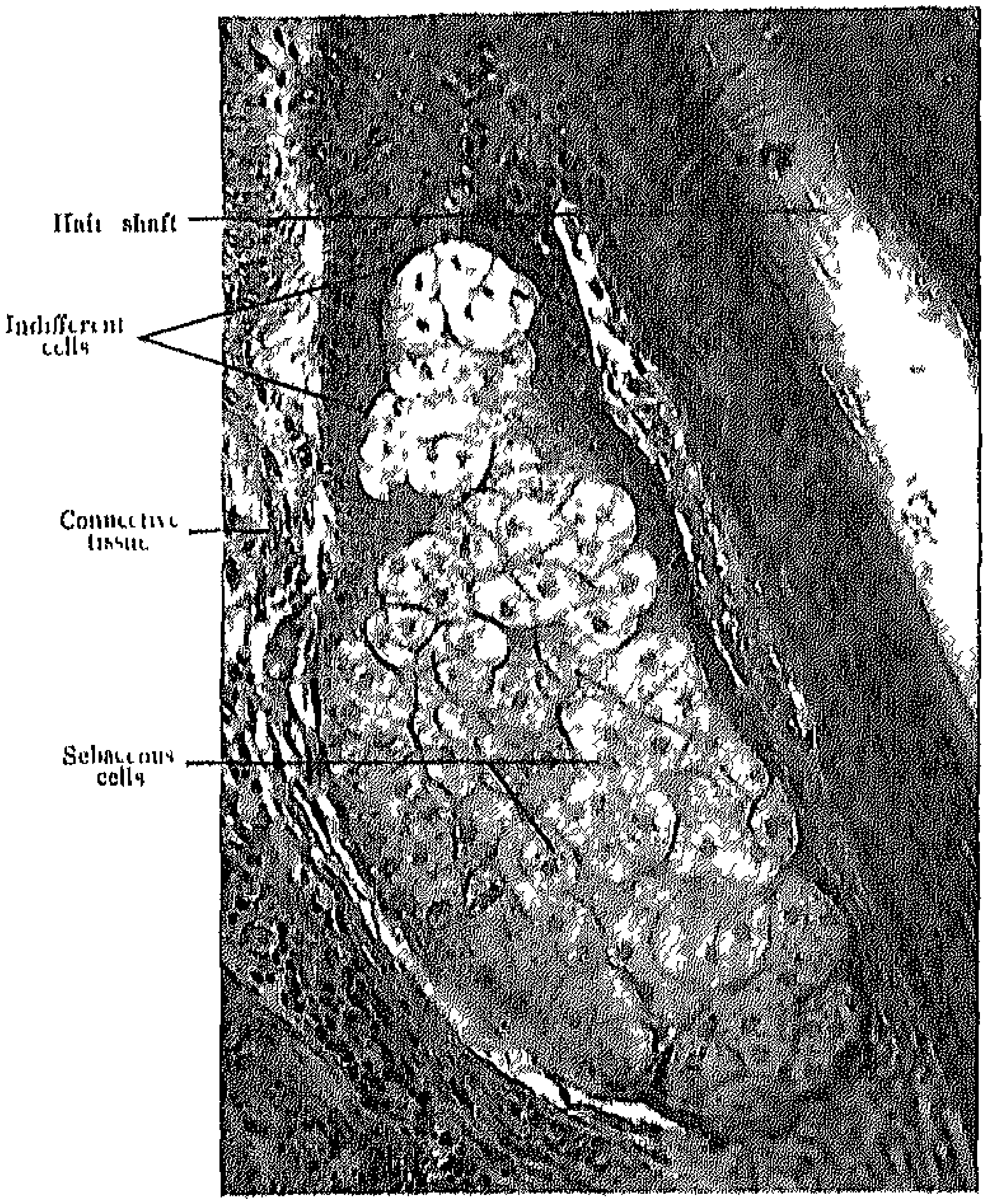


Fig. 213. Section of a human sebaceous gland from the scalp. Photomicrograph.

cells of the lower part of the inner root sheath are also cornified and become attached to the lower end of the root, which is separated from the bulb. This enlargement of the root gives it a clublike appearance and these hairs are known as *club hairs*. As the club hairs are separated from the bulb, they pass upward into the neck of the follicle where they remain for a longer or shorter period, depending on whether they are pulled out or are pushed out by the new hair growing up from below. In the meantime, the cells of the outer root sheath grow inward, a new bulb and matrix are formed, and a new hair begins to develop by the usual process of growth.

The blood supply of the hair follicles is by small arteries which ascend into the papillae in the form of capillary networks. Branches from the subpapillary plexus also form capillary loops which are closely applied to the hyalin membranes of the follicles. The veins which return the blood from the papillae join larger vessels in the subcutaneous tissue. The veins from the capillaries about the follicles join the venous networks in the corium.

The nerves are mainly myelinated fibers which lose their sheaths and break up into delicate branches that end in enlargements on the surface of the hyalin membranes. Small, disclike epithelial structures are located close to the hairs as they emerge from the skin. These discs are said to receive nerve fibers and are regarded as being sensory in character. Unmyelinated fibers supply the walls of the blood vessels and of the glands.

The vibrissae or large tactile hairs of certain animals receive fibers which penetrate the hyalin membranes and end in relation to specially modified cells in the outer root sheath. Hairs are also very important touch organs in man

THE NAILS

The nails are flattened, platelike structures located on the dorsal surfaces of the distal ends of the digits. Each nail consists of an exposed portion, the *body*, and a portion which is embedded in the skin, the *root*. Distally the nail ends in a free edge which overlies the tip of the digit. The folds formed by the skin on the lateral borders of the nail are known as the *nail wall*, while the portion of the skin that is folded over the root is called the *nail fold*.

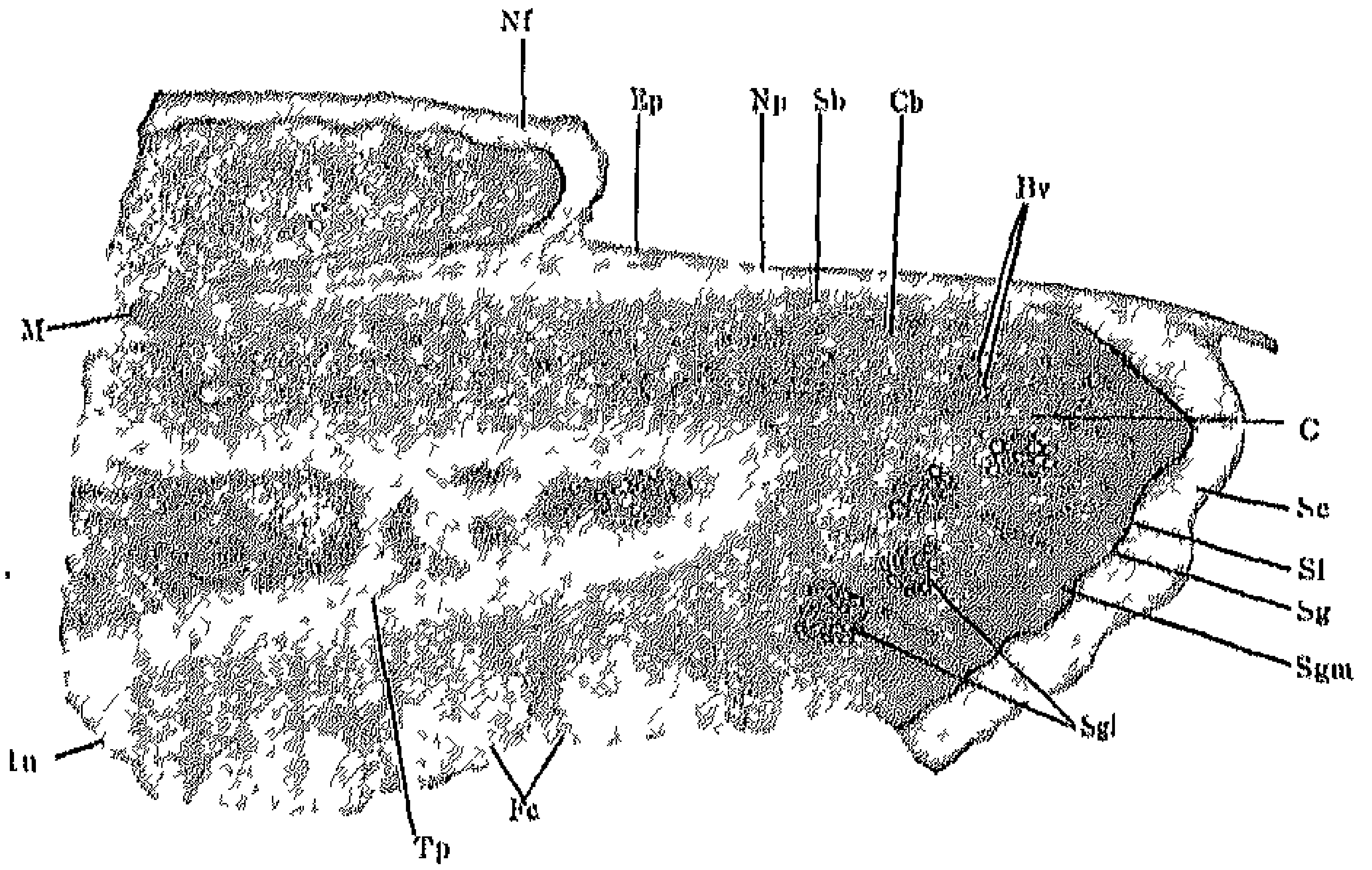


FIG. 214. Longitudinal section through the tip of the finger. (Nf) Nail fold. (Ep) Eponychium. (Np) Nail plate. (Sb) Stratum germinativum of the nail bed (epidermis) (Cb) Corium of the nail bed. (Bv) Blood vessels. (Sgl) Sweat glands (Tp) Terminal phalanx of the finger (Tn) Tendon. (M) Matrix. (Fc) Fat cells. (C) Corium (Sgm) Stratum germinativum. (Sg) Stratum granulosum. (Sl) Stratum lucidum. (Sc) Stratum corneum.

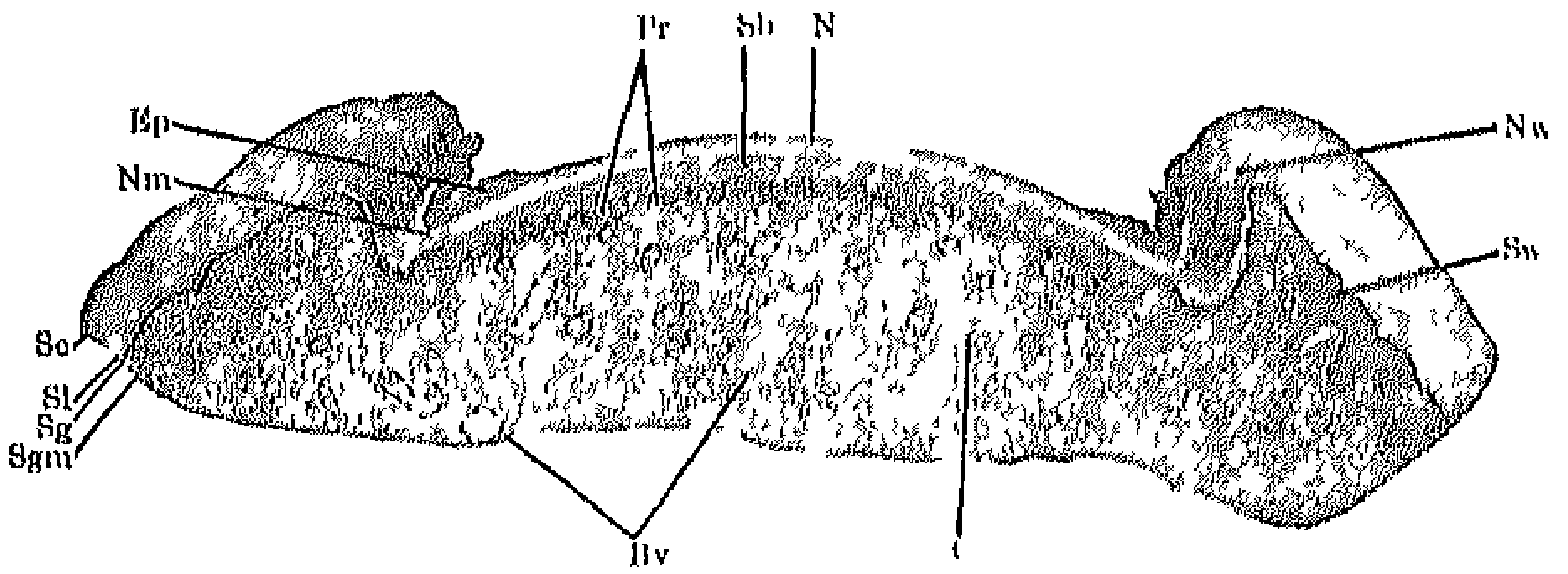


FIG. 215. Transverse section of a finger nail. The drawing has been shortened slightly from side to side to preserve relations (N) Nail plate (Sb) Stratum germinativum of the nail bed (Pr) Papillary ridges of the nail bed (C) Corium (Nw) Nail wall (Sw) Stratum germinativum of the nail wall (Ep) Eponychium (Nm) Margin of nail. (Bv) Blood vessels. (Sc) Stratum corneum (Sl) Stratum lucidum. (Sg) Stratum granulosum. (Sgm) Stratum germinativum

The *nail*, or *nail plate*, is a hard structure consisting of cornified cells closely bound together and arranged in overlapping lamellae. The underlying tissue on which the nail rests is called the *nail bed* and consists of an epithelial portion and a corium. The epithelial portion is continuous with the stratum germinativum of the skin. It passes over the tip of the digit and forms a thin layer of epithelial cells beneath the nail plate. The epithelial layer and the nail plate are so closely related that they are called, by some authorities, the soft and hard parts of the nail. The epithelial layer increases in thickness beneath the root and forms the *matrix*, the position of which is indicated, especially after the nail fold has been pushed back, by a white, crescentric area, the *lunula*.

The corium forms the deep portion of the nail bed. It consists of densely interwoven collagenous and elastic fibers arranged in bundles, some of which extend from the epithelium to the periosteum. The papillae beneath the epidermis on the tip of the digit, form a series of longitudinal ridges beneath the epithelial layer of the nail bed.

The lateral borders of the nail lie in a groove between the nail bed and the nail wall. This is known as the *nail groove*. The skin which forms the nail fold turns inward above the root of the nail, its stratum corneum extending forward from beneath the nail fold as a ragged membrane, the *eponychium*.

The cells of the epithelial layer of the nail bed in front of the lunula do not contribute to the formation or growth of the nail plate. The nail plate increases in thickness by the addition of cells which have become cornified and added to the portion of the root lying upon the matrix. The cells about the proximal border of the root undergo a similar transformation and are added to it from behind. With the addition of this new material, the body of the nail is pushed forward over the nail bed as it increases in length.

THE MAMMARY GLANDS

The mammary glands, although functionally related to the organs of reproduction, are modified cutaneous structures. They are present in both sexes, in the same degree of development up to the time of puberty, after which the glands atrophy in the male. In the female they continue to develop and become functional after pregnancy when the period of active lactation begins.

The glands are contained in the *mammae*, which are rounded, hemispherical bodies of varying degrees of prominence. The glandular elements are surrounded by a considerable amount of loosely arranged connective tissue with which masses of fat are intermingled. The central portion of the mamma is elevated to form the *nipple*, which is located in the middle of a more or less deeply colored area, the *areola*. The epidermis covering the nipple and the areola is deeply papillated and contains a considerable amount of pigment, which assumes a deeper color after the first pregnancy. A number of small bundles of smooth muscle fibers are disposed in the skin beneath the areola and about the nipple. At the base of the nipple these fibers are arranged in a circular fashion, some of the bundles extending into the structure. By the action of these muscular fibers the nipple is extended and elevates. Small, rudimentary glands which are structurally similar to the mammary glands are present in the skin beneath the areola, their position being indicated on its surface by small rounded elevations. These glands are known as the *areolar glands of Montgomery*.

The mammary gland consists of 15–20 groups or lobes of glandular elements, separated from one another by fibrous septa (interlobar septa). From these interlobar septa the connective tissue extends into the lobes dividing them into lobules (interlobular septa). From the interlobular septa very thin septa (intralobular septa) extend into the lobules to act as the supporting tissue for the glandular epithelium. In both the interlobar and the interlobular septa the connective tissue is dense and made up almost exclusively of compactly arranged bundles of collagenous fibers. Elastic fibers are few and scattered. Cellular elements are reduced in number. In certain areas fat cells may be present in quantity. On the other hand, the intralobular connective tissue is almost the opposite of this. The cells are numerous, the quantity of fibers is reduced markedly and those that are present are fine and delicate, a condition which allows for the expansion of the glandular tissue as it changes from the nonfunctional to the functional state. Fat is seldom, if ever, present. Numerous blood vessels are present in the more loosely arranged tissue, together with lymphocytes, histiocytes and plasma cells. The presence of granular leucocytes is usually regarded as indicating an inflammatory condition.

In general, the structure of the inactive mammary gland presents a picture in which the connective tissue elements predominate, the glandular elements consisting mainly of ducts and their branches. The whole appearance of the gland is that of a scattered collection of branching tubes, widely separated by broad septa of connective tissue.

In the inactive gland the alveoli or secreting elements are small and undeveloped, the lobes consisting mainly of the single *lactiferous duct* and its branches, which pass from each lobe to open into a small depression in the summit of the nipple. In the lobe, the branches of the principal duct end in small, collapsed alveoli or in cordlike masses of cells from which alveoli are developed when the gland becomes active. These glandular elements are widely separated by the interlobular and interlobar connective tissue.

The walls of the alveoli consist of cuboidal cells which rest on a basement membrane. Between the epithelial cells and the basement

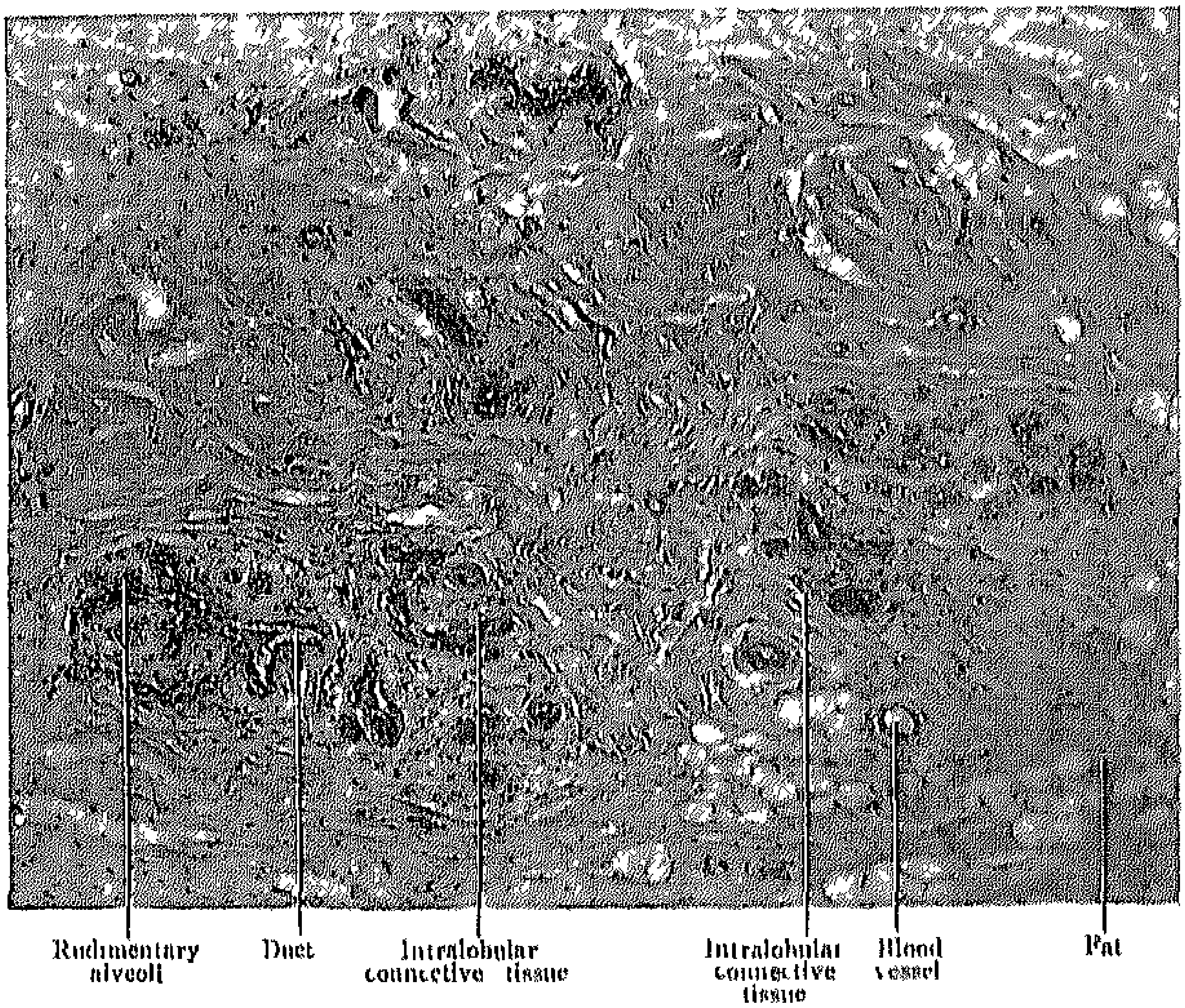

Rudimentary alveoli
Duct
Intralobular connective tissue
Intralobular connective tissue
Blood vessel
Fat

Fig. 216. Section through an inactive mammary gland of a five year old girl. Photomicrograph.

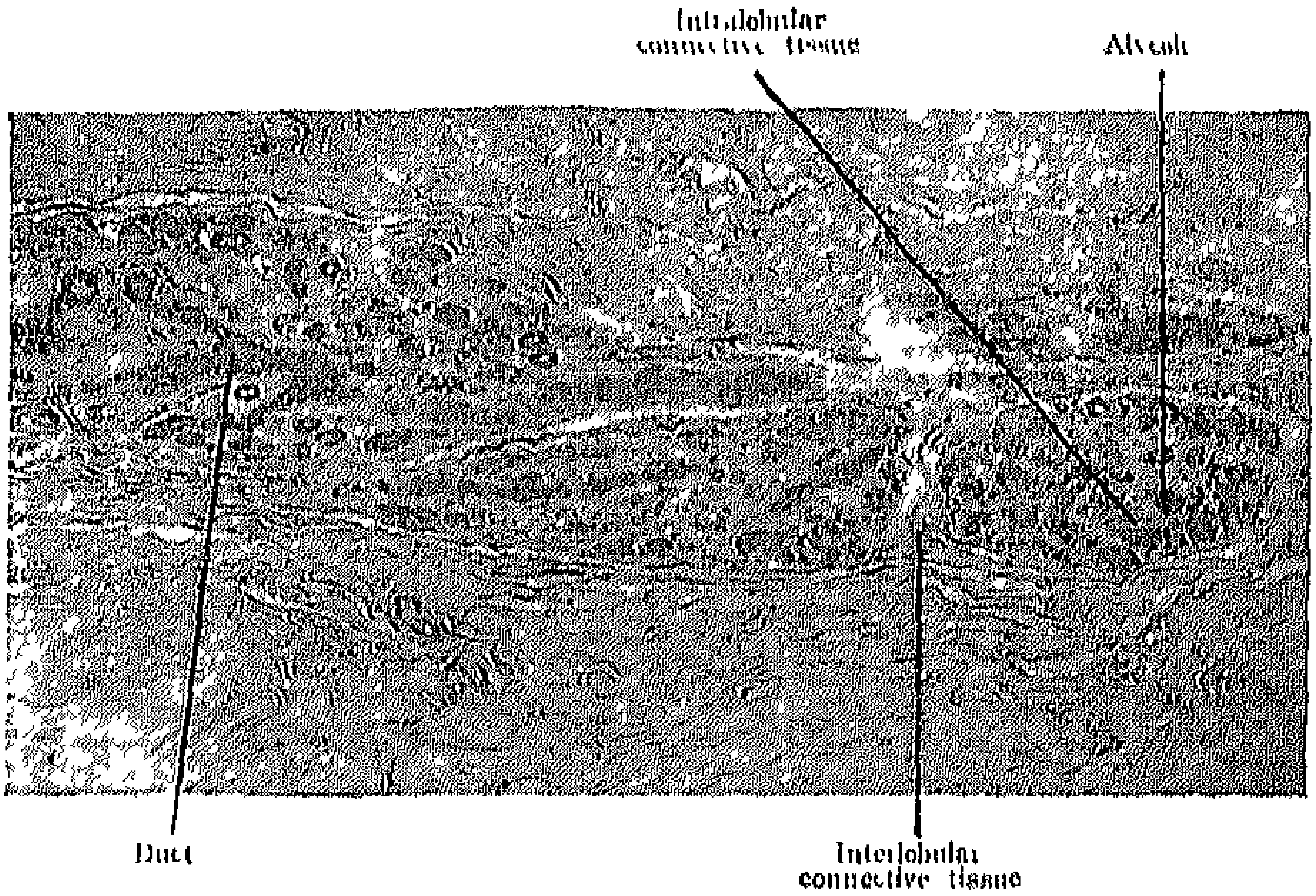

Intralobular connective tissue
Alveoli
Duct
Interlobular connective tissue

FIG. 217. Section through the mammary gland during the early months of pregnancy. Photomicrograph.

membrane are numerous delicate, spindle-shaped myoepithelial cells which do not form a continuous layer and are looked upon as muscular elements.

The smaller ducts present about the same structure as the alveoli, that is, they are lined by a cuboidal epithelium with myoepithelial elements between the epithelial cells and the basement membrane. These contractile elements are more abundant in the ducts than in the alveoli and by their contraction aid the passage of the secretion. The larger ducts are lined by a simple columnar epithelium; the epithelium lining the still larger ducts being stratified columnar. Beneath the areola, the lactiferous ducts form spindle-shaped expansions, the *ampulla* or *lactiferous sinuses*. These enlargements serve for the storage of a reserve supply of the secretion of the glands. The ducts narrow somewhat from the ampullae to the point where they open into the nipple and are lined by a stratified squamous epithelium, which is continuous with the epithelium of the skin. Since there is a lactiferous duct for each lobe, from 15–20 ducts open into the depression at the summit of the nipple.

Toward the end of pregnancy a marked change takes place in the structure of the gland. The collapsed alveoli begin to enlarge and expand. The ducts send out new branches, some of which end in alveolar enlargements, others end in cords and masses of epithelial cells which soon acquire lumina and become alveoli. As this increase and expansion of the glandular elements continues, the connective tissue is compressed into very thin septa between the alveoli.

The cells of the alveoli in the actively lactating gland are cuboidal at first. With the development of fat globules they become columnar and tend to project into the lumen of the alveolus. The fat first appears as small granular bodies which stain black with osmic acid. These granules combine and form droplets, the droplets coalescing to form a large globule close to the free surface of the cell. The fat globules are finally discharged into the lumen of the alveolus by the rupture of the outer portion of the cell (apocrine manner of secretion). They are mingled in the alveolus with an albuminous fluid which is secreted by the cells of the alveolar epithelium. After the fat globules are discharged, the cell reorganizes and the process is repeated.

In sections of functional mammary glands, the alveoli in different lobules and sometimes alveoli in the same lobule appear to be in

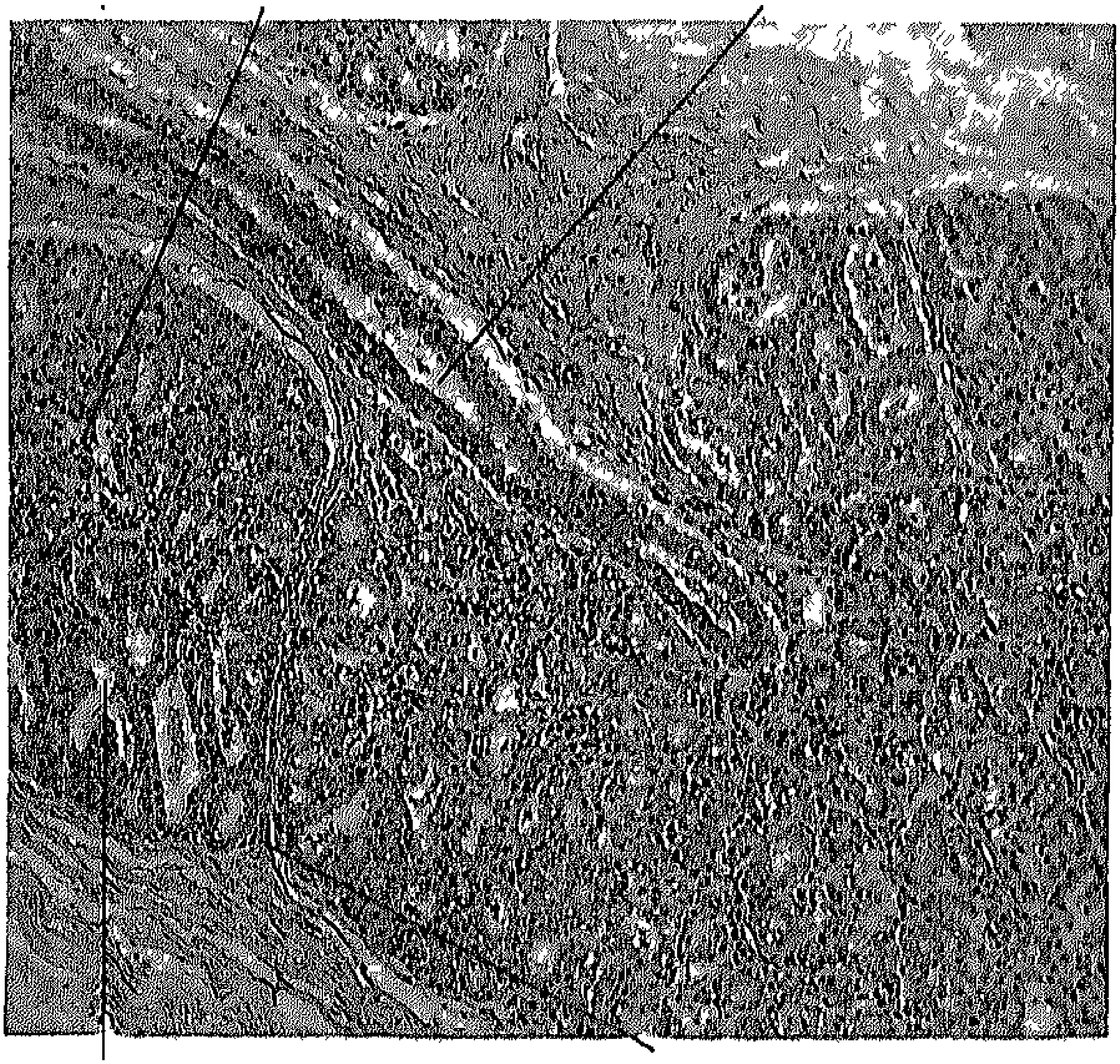

Intralobular connective tissue
Duct
Alveolus
Interlobular connective tissue

FIG. 218. Section through a lactating mammary gland (human). Photomicrograph.

different conditions of activity. In some alveoli the cells are columnar and are filled with fat droplets, while in others they are cuboidal and give no visible evidence of a secretory activity. This is due to the fact that the alveoli pass through periods of activity, alternating with periods of rest, hence all of the alveoli observed in a single section do not present the same functional condition. The walls of some of the alveoli may be so distended by the amount of secretion they contain that their cells are reduced to thin, flattened elements.

Growth and development of the mammary glands and the production of milk are under control of endocrine secretions from the ovary and the pituitary glands. Estrogen, produced by the granulosa cells of the ovary (and also by the placenta), stimulate the growth and development of the duct system. Progesterone (produced by the corpus luteum and the placenta) causes the alveoli to develop and enter the presecretory stage from which, in the presence of prolactin from the anterior pituitary, they go on to the full lactation stage.

The secretion of the gland is called *milk*. It is an emulsion of fat droplets suspended in a clear, watery fluid which contains in solution albuminous substances, sugar and inorganic salts. This fluid is secreted by the cells of the alveoli, but the fat droplets are believed to be taken out of the surrounding fluids by the cells and are not elaborated in their cytoplasm. During the last days of pregnancy and for a few days after it has terminated, the glands produce a clear, watery fluid, the *colostrum*. Colostrum differs from milk in the small amount of fat which it contains. Numerous bodies, the *colostrum corpuscles*, are characteristically present. The corpuscles are usually spherical, although they may be quite irregular in form. They are believed to be large, phagocytic cells which have become distended with particles of ingested fat.

At the end of the period of lactation a series of retrogressive changes *(involution)* takes place. The glandular structures are greatly reduced or disappear, the connective tissue elements increase and there is a return of the gland to its nonfunctional condition. However, this return is not absolute, since some of the alveoli may remain and may even be capable of secreting for some time.

After the menopause the glandular elements are still further reduced, and in advanced age may become fibrous cords. The connective tissue of the gland undergoes retrogressive changes and the entire structure becomes reduced and shrunken.

At first the blood vessels are distributed about the surface of the gland; branches from these superficial vessels follow the interlobar and interlobular connective tissue into its deeper portions where their branches form networks about the alveoli. The veins leave the glands by following the course of the arteries. The supply of blood to the gland is greatly increased during the period of lactation.

The lymphatics arise as capillaries about the alveoli. These capillaries unite to form the smaller lymphatics which join the large lymphatics in the interlobar tissue. For the most part, the lymphatic vessels leave the gland to empty into the axillary nodes.

The nerve supply is mainly from the sympathetic centers, their fibers ending in the walls of blood vessels and terminating in the form of fine plexuses about the alveoli. It is said that a few fibers penetrate the basement membrane of the secreting structures and end between the cells.

20

The Male Reproductive Organs

The organs belonging to the male reproductive system are: the *testis, epididymis, ductus deferens* and the *penis*. Associated with these structures are certain accessory organs, namely, the *seminal vesicles*, the *prostate gland*, and the *bulbourethral glands*.

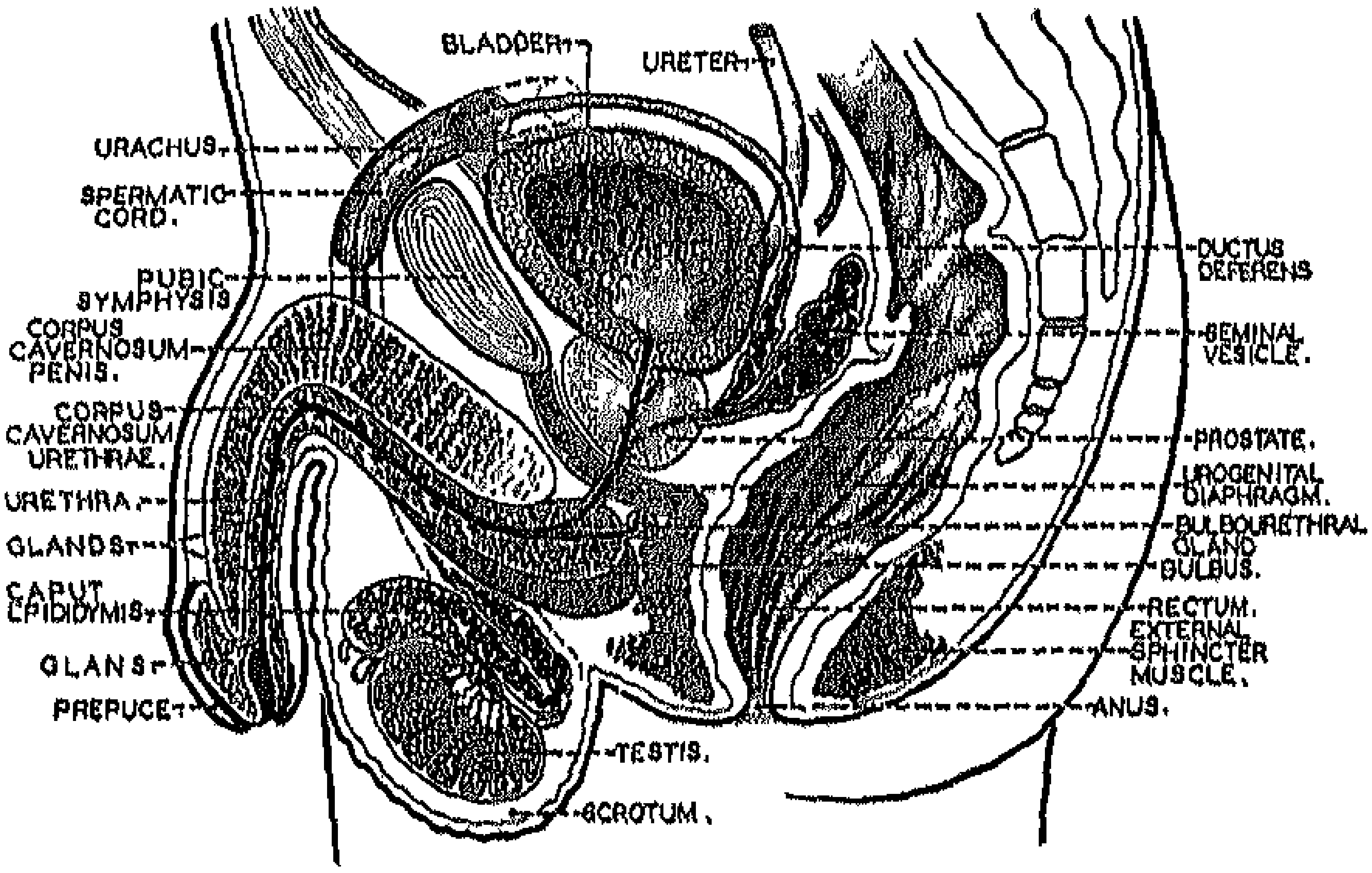


FIG. 219. The urogenital system (male). The glandular complications of the male urogenital system appear to be in part an adaptation to the double function of the urethra—excretory and reproductive. The alkaline secretions of the glands serve to neutralize the acidity of the urethra caused by the acid urine. (Sobotta.) (Courtesy, Neal and Rand: "Comparative Anatomy," Philadelphia, The Blakiston Company.)

THE TESTIS

The male germ cell or sperm is produced in the testis. Organs in which cellular elements such as the spermatozoa and the ova are developed are known as *cytogenic glands*. The glandular character of the testes, however, is not determined by their production of spermatozoa alone, since they are also the source of certain substances called *hormones* which are delivered directly to the blood. They are, therefore, to be classed also with the ductless glands.

The testes are egg-shaped, glandular bodies that are suspended by means of the spermatic cords in a membranous sac, the *scrotum*.

At first the testes lie in the abdominal cavity. A saclike diverticulum, the *processus vaginalis*, is formed by a downgrowth of the peritoneum into the scrotum. The processus vaginalis is accompanied by the structures of the abdominal wall through which it passes. Each testis follows the processus into the scrotum, being aided in its descent

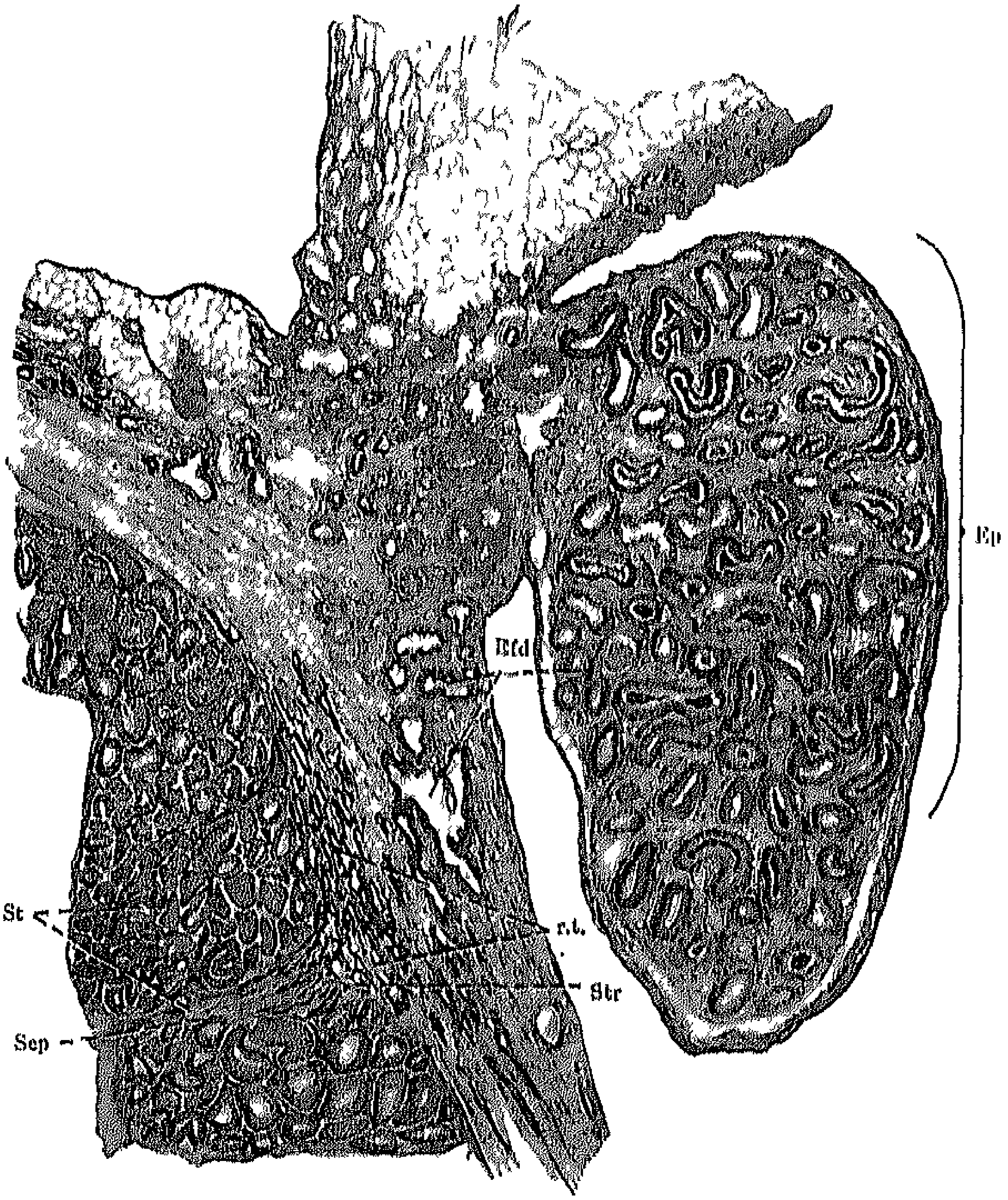


FIG. 220. Testis, mediastinum testis, and epididymis. (St) Seminiferous tubules. (Sep) Septula testis. (Str) Straight tubules (tubuli recti). (r.t.) Rete testis in mediastinum. (Efd) Efferent ducts. (Ep) Epididymis.

by the shortening of a fibrous cord, the *gubernaculum testis*, which extends from the posterior end of the testis into the scrotal sac. After the testis is lodged in the scrotum the upper part of the processus is shut off, thus closing its communication with the abdominal cavity. Its saclike portion in the scrotum folds about the anterior and lateral sides of the testis, forming an investing covering, the *tunica vaginalis*. The tunica vaginalis consists of two layers: a parietal layer which is applied to the inner surface of the wall of the scrotum, and a visceral layer which forms the outer covering of the wall of the testis. The two layers are separated by a serous cavity, which is derived from the processus vaginalis.

The testis is enclosed in a thick capsule, the *tunica albuginea*, composed of densely compacted collagenous and elastic tissue, in which the elastic fibers predominate. The number of elastic fibers increases with age. Beneath the tunica albuginea is a more loosely arranged layer of connective tissue which supports numerous blood vessels. It is known as the *tunica vasculosa*. This layer is more evident in early life. Later it loses much of its vascular character and can hardly be distinguished from the rest of the tunica albuginea. The tunica albuginea is greatly thickened posteriorly and forms the *mediastinum testis* or *body of Highmore*. From the mediastinum, connective tissue extends out to form diverging septa *(septula testis)* which attach to the tunica albuginea of the opposite wall. These septa divide the testis into a series of about 250 compartments, known as the *lobuli testis*. These lobules are roughly pyramidal in shape, their narrow portions being toward the mediastinum, their broader, basal portions being directed peripherally.

Each lobule contains from one to three tubular structures, the *seminiferous tubules (convoluted tubules)*. After winding about in a series of complicated coils the ends of the tubules do not end blindly, but anastomose and form loops, an arrangement which provides for the exit of the spermatozoa in case obstructions should be formed in some of the tubules. Occasionally tubules may pass through the intervening septula and join those in the adjacent lobules. The tubules are supported by delicate fibers which extend into the lobule from the septula and form the interstitial connective tissue. These fibers not only bind the tubules together, they also give support to the blood vessels by which they are supplied.

As the convoluted tubules pass toward the mediastinum they become continuous with the *straight tubules (tubuli recti)*. As the straight tubules continue toward the epididymis they form thin-walled, anastomosing spaces in the mediastinum known as the *rete testis*. Occasionally a single convoluted tubule may join the rete directly. The rete testis communicates with the duct of the epididymis by 15–20 tubules,

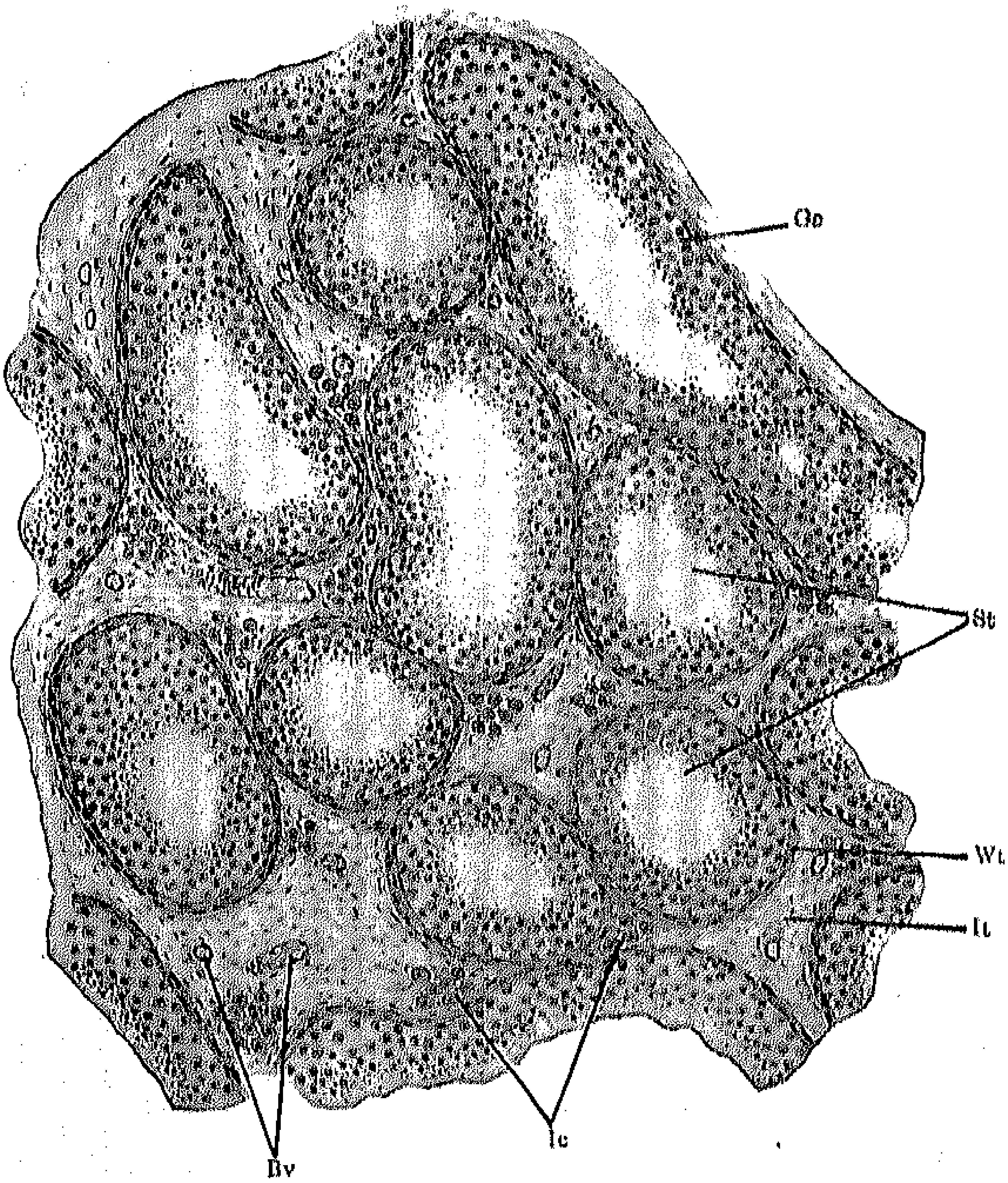


FIG. 221. Section through the convoluted (seminiferous) tubules of a human testis. (St) Seminiferous tubules. (Ge) Germinal epithelium. (Wt) Connective tissue wall (tunica albuginea) of a tubule. (It) Interstitial tissue. (Ic) Interstitial cells. (Bv) Blood vessels.

known as the *efferent ducts (ductuli efferentia).* Passing into the head of the epididymis *(globus major)* these ducts pursue a straight course for a short distance, they then enlarge, become convoluted and assume a cone-shaped arrangement, the *coni vasculosi,* which unite with the *ductus epididymis.* The ductus forms a series of coils, which continue through the body to the globus minor where it joins the *vas deferens.*

THE SEMINIFEROUS TUBULES. The wall of a seminiferous tubule consists of an outer layer of closely interwoven collagenous and elastic fibers containing flattened fibroblasts, a thin basement membrane on which rests the highly specialized spermatogenic epithelium made up of two types of cells: the supporting cells *(cells of Sertoli)* and the germinal *(spermatogenic)* cells.

The cells of Sertoli are slender, protoplasmic columns extending from the basement membrane to the surface of the epithelium. Their large, pale, vesicular nuclei are oval in outline and are located at different levels. Their cytoplasm has a reticulated appearance and contains granules, fat droplets and pigment. A crystalloid body is usually located near the nucleus. Mitochondria can be demonstrated by the use of special staining methods. The sides of these cells show a marked irregularity due to the indentations made by the pressure of the adjacent spermatogenic cells. The cells of Sertoli may degenerate, but apparently undergo division only rarely. They furnish support and nourishment for the developing spermatogenic cells.

The spermatogenic cells occupy the spaces between the Sertoli cells and form an epithelium which may be several cell layers in thickness. These cell layers represent the different stages in the development of

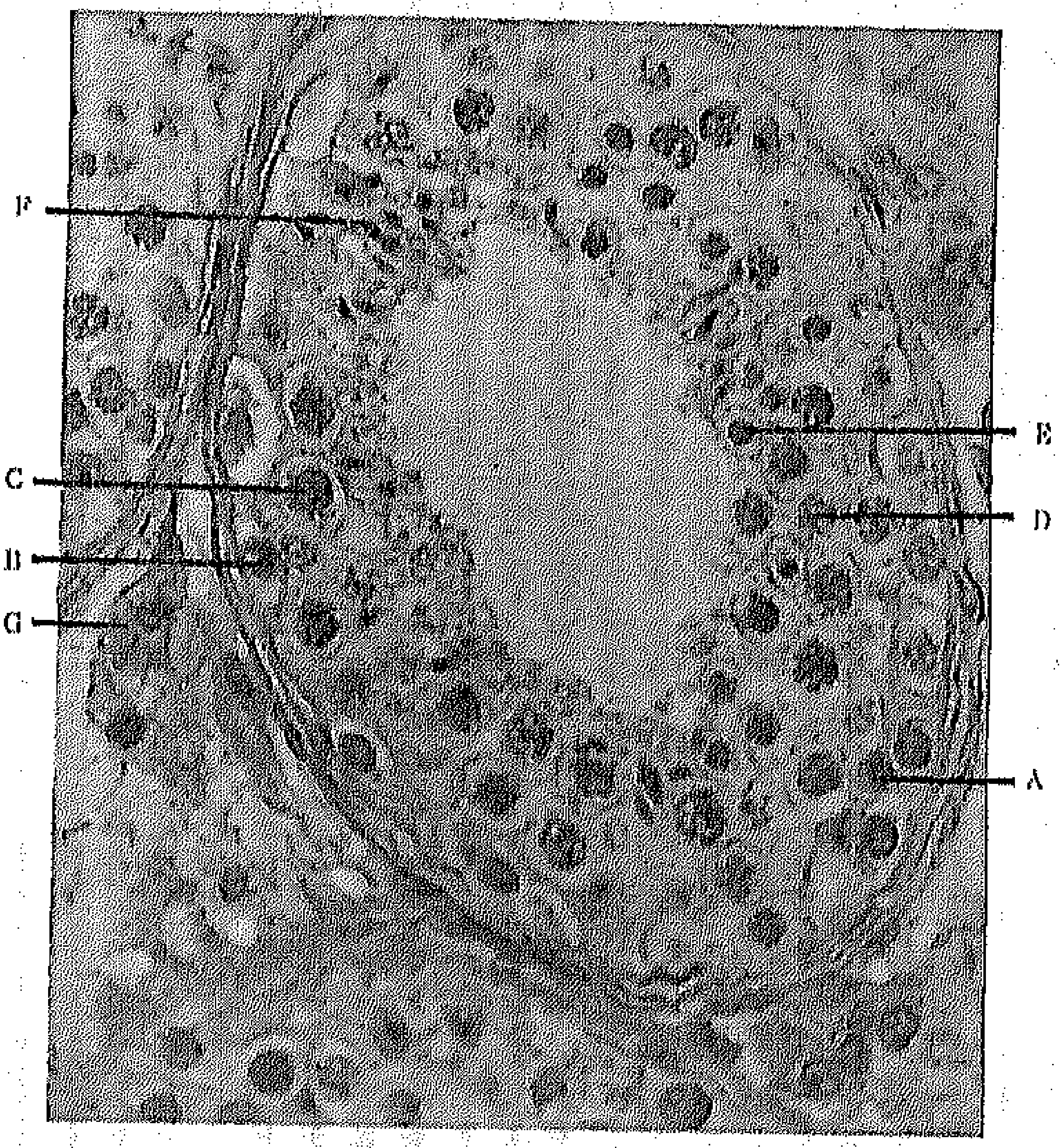


FIG. 222. Section through a seminiferous tubule (human). (A) Sertoli cell. (B) Spermatogonia. (C) Primary spermatocyte. (D) Secondary spermatocyte. (E) Spermatid. (F) Spermatozoa. (G) Interstitial cells. Photomicrograph.

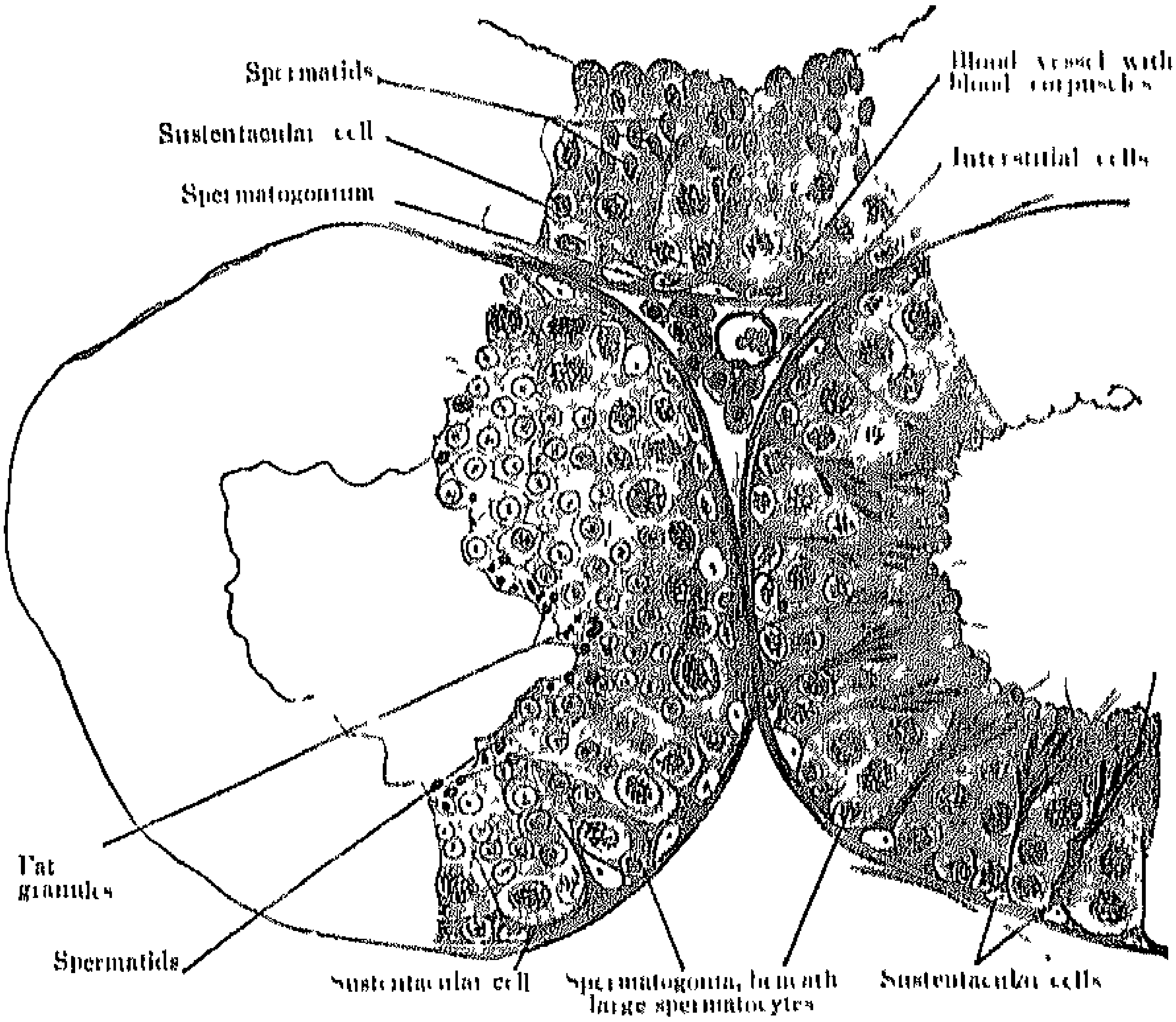


FIG. 223. Cross section of seminiferous (convoluted) tubules of a mouse. 360 ×. (Courtesy, Bremer-Weatherford: "Textbook of Histology." Philadelphia, The Blakiston Company.)

the spermatozoa. Proceeding from the basement membrane to the lumen of the tubule, the cells which compose these layers are the *spermatogonia*, the *primary* and *secondary spermatocytes*, the *spermatids*, and the final product of the divisions and transformations which take place among the cells of the germinal epithelium, the *spermatozoa*.

The spermatogonia are cuboidal or subspherical cells which lie directly on the basement membrane, comprising two or three layers, as a rule. The nuclei are spherical and the chromatin is usually in the form of a closely meshed network. The spermatogonia produce a succession of similar cells by repeated divisions. After several generations of cells have been produced in this manner, some of the spermatogonia pass through a period of growth and become spermatocytes.

The primary spermatocytes are considerably larger (17–19 microns, compared to 12 microns for spermatogonia) than the spermatogonia. The chromatin in their large vesicular nuclei presents a variety of patterns according to the stage of activity in which the cell finds itself. These cells form the two or three layers internal to the spermatogonia.

The secondary spermatocytes are smaller (12–14 microns) than the primary spermatocytes, from which they are derived by mitotic division. The spherical nuclei stain deeply owing to the condensation of their chromatin. These cells form one to three layers internal to the primary spermatocytes and give rise, almost immediately, to the spermatids.

The spermatids are small cells with deeply staining, spherical nuclei. They do not divide, but are lodged in the protoplasm of the cells of Sertoli where they undergo a process of transformation by which they become spermatozoa.

The nucleus of the spermatid shifts to one pole of the cell, the cytoplasm of which becomes narrow and elongated. The centrosome divides into two parts, of which the proximal part remains close to the nuclear membrane. The distal centrosome moves a short distance from the proximal part and divides again A threadlike filament grows from the first piece of the distal centrosome and continues to increase in length until, as the axial filament, it extends for some distance beyond the cytoplasm. The second piece of the distal centrosome forms a ring about the axial filament and moves to the pole of the cytoplasm opposite the nucleus.

The cytoplasm between the proximal centrosome and the first piece of the distal centrosome, becomes constricted and forms the neck. Between the first and second pieces of the distal centrosome, it is reduced to a narrow cylinder, the body. A portion of the cytoplasm is condensed about the axial filament and forms the spiral filament. The axial filament continues to grow beyond the cytoplasmic body and develops a thin membrane about its proximal three-fourths, its distal fourth remains uncovered.

The changes referred to above take place while the cell (spermatid) is embedded in the cell of Sertoli. After the transformation is completed, the spermatozoon frees itself and passes from the tubule to the epididymis in which it is stored.

The spermatozoon, when viewed with ordinary magnifications, is seen to consist of a *head*, a middle piece or *body*, and an end piece or *tail*. The head is oval in outline when seen in direct view and pear-shaped when seen in profile. The middle piece has the form of a protoplasmic cylinder, while the end piece or tail is a long, vibratile filament. When specially prepared material is observed with the highest magnifications, the head is seen to consist of a mass of deeply stained material, the condensed chromatin of the nucleus of the spermatid. Its anterior third or more is covered by a structureless membrane, the *galea capitis*, its anterior border presenting a sharpened edge, the *perforatorium*. The middle piece or body is connected with the head by a short, constricted portion, the *neck*. The proximal centrosome forms a thickened disc, located at the point where the neck is attached to the head. This is known as the *anterior end knob*. Located at the point of attachment of the neck to the body, is a similar disc known as the *posterior end knob*. This is the first part of the divided centrosome. The *axial filament* begins at the posterior end knob, extends through the body and continues as the vibratile tail of the spermatozoon. At the point where the filament leaves the body, it passes through a ringlike disc, the *end ring*, which is formed by the second part of the distal centrosome. Between the posterior end knob and the end ring, the protoplasm is condensed to form a spiral filament which is closely wound about the axial filament. The tail consists of a proximal portion or chief piece, in which the axial filament is enclosed by a thin, protoplasmic membrane for about three-fourths of its length. In the remaining fourth or terminal piece of tail, the axial filament remains uncovered.

The connective tissue forming the inner loose vascular layer of the capsule is continued into the testis and around the seminiferous tubules where it forms the stroma of the organ. There is relatively little interstitial tissue. Through it run blood and lymph vessels and nerves. It also contains the cells usually associated with a loose connective tissue together with the specialized *interstitial cells* of the testis *(cells of Leydig)* which are concerned with the elaboration of the male sex hormone, *testosterone*. The latter plays an important role in the development and function of the secondary sexual characteristics and in the development of sexual instincts. These interstitial cells are considered to be of mesenchymal origin, since they arise from cells which cannot be distinguished from ordinary fibroblasts. The interstitial cells occur singly or in groups between the seminiferous tubules. They are large cells, polyhedral in shape and in man they vary in size from 14–20 microns. Each cell usually contains a single large, round, vesicular nucleus (occasionally cells with more than one nucleus may be observed) with one or more nucleoli. The cytoplasm is abundant and contains granules and other inclusions. Coarse lipoid granules are found in abundance in the peripheral portions of the cytoplasm and are thought to contribute to the formation of androgenic hormone. Other finer granules are distributed around the nucleus. Also included in the cytoplasm of these cells are mitochondria and, less constantly, brown pigment granules and rod-shaped crystalloids. In fully developed interstitial cells mitotic figures are almost never encountered.

SPERMATOGENESIS. The production of spermatozoa by the division and transformation of the spermatogenic cells in the seminiferous tubules is called spermatogenesis. The process of spermatogenesis does not take place in all seminiferous tubules or in all parts of the same tubule, simultaneously. The spermatogenic epithelium may be active in portions of the tubules, while in the other portions the spermatogenic cells are in a condition of rest.

Not only does spermatogenesis result in the production of a highly specialized cell, but also of one in which the chromatic material has been reduced to the amount represented by one-half of the usual number of chromosomes.

The spermatogonia are equipped with the full (diploid) number of chromosomes (48 in man). During the period of growth, the chromosomes unite in pairs so that the number in the primary spermatocytes is one-half that in the spermatogonia (haploid number). Each chromosome, however, consists of two of the original chromosomes which have been joined together (synapsis).

When the primary spermatocytes prepare to divide, each double chromosome again separates in a longitudinal plane and splits transversely, forming four chromosomic bodies which are known as a *tetrad*. When the primary spermatocyte divides, a *dyad* (two chromosomic bodies) from each tetrad passes into each of the resulting spermatids. In the division of a secondary spermatocyte, a *monad* (a single chromosomic body) from each dyad passes into each of the resulting spermatids. Thus each spermatozoon resulting from the transformation of a spermatid carries to its union with an ovum the amount of chromosomic material which represents one-half of the chromosomes of the original cell.

The diploid number of chromosomes in the human germ cell is 48. Of these chromosomes X and Y are known as the sex chromosomes.

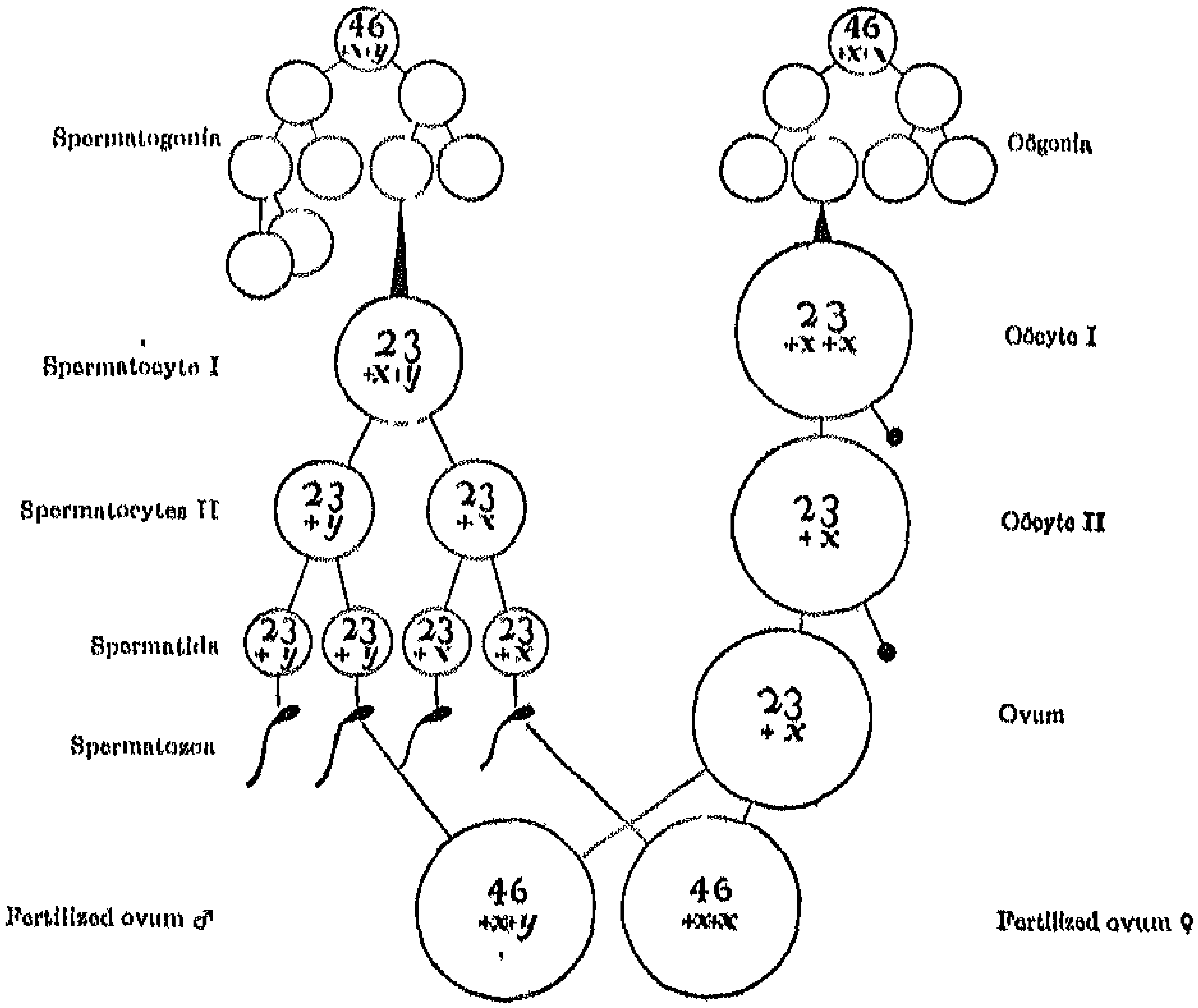


FIG. 224. Diagram of spermatogenesis, oögenesis, and fertilization. Chromosome numbers are those for man. (Courtesy, Bremer Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

The sperm, after its reduction to the haploid number, contains the material of 24 chromosomes, one of which is either X or Y. The ovum after reduction has the material of 24 chromosomes, one of which is always X. When the sperm, uniting with the ovum, carries an X chromosome, the resulting individual is a female. On the other hand, if the sperm carries a Y chromosome, the individual developing from this union will be a male.

The testes are supplied by branches of the internal spermatic artery. These branches enter through the mediastinum and pass in the septula to the points where they invade the lobules, in which they form capillary networks about the tubules.

The testes are abundantly supplied with lymphatics which arise in the interstitial tissue and pass in the septula to the mediastinum. There they join larger lymph vessels which pass out in the spermatic cord.

The nerves follow the course of the blood vessels into the interstitial tissue, where they break up into fine branches which are distributed to the walls of the vessels and to the tubules.

SPERMATIC DUCTS

The spermatic ducts are the tubes which convey the spermatozoa from the seminiferous tubules to the point where they are discharged

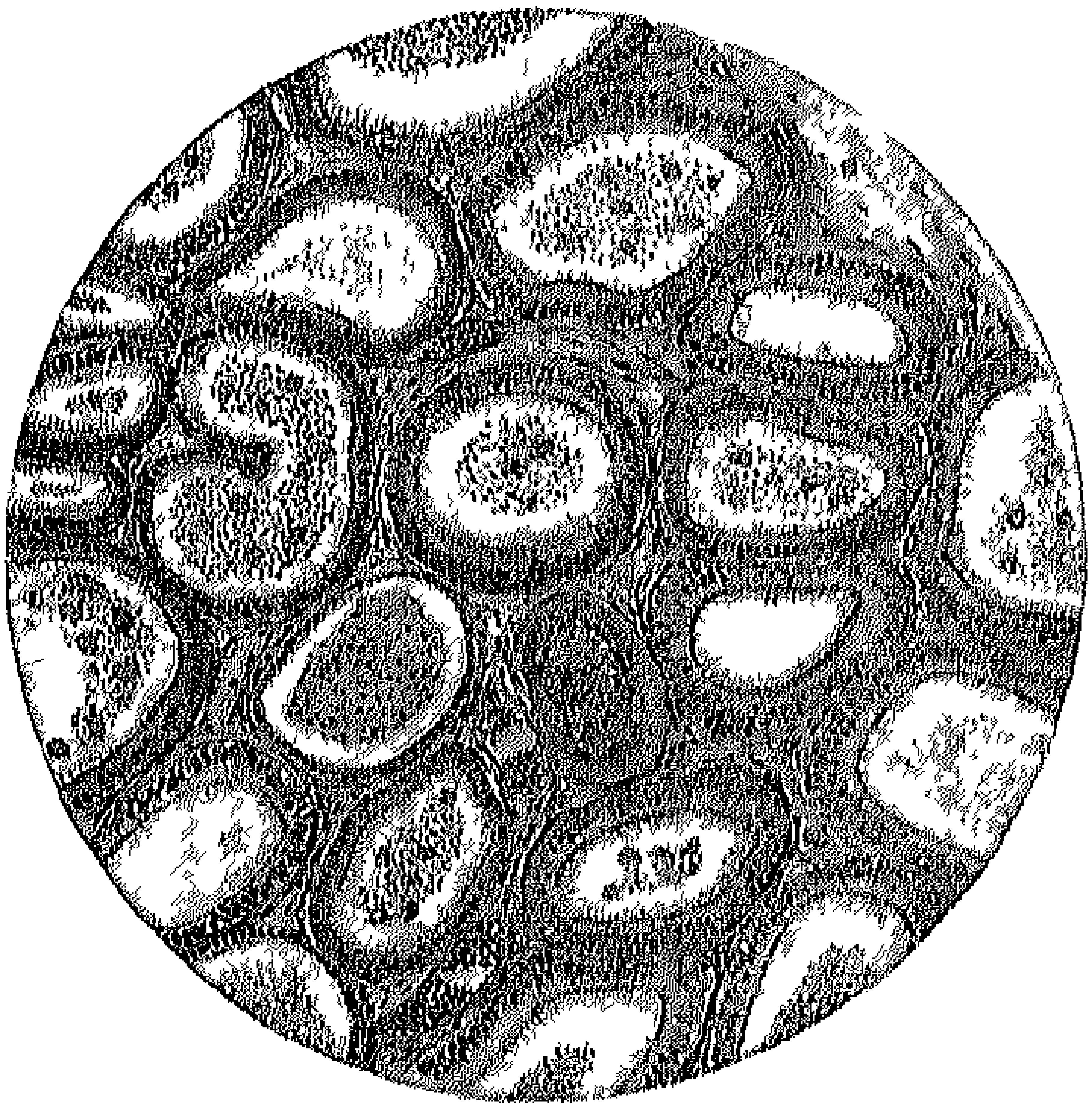


FIG. 225. Sections through the coils of the ductus epididymis.

into the prostatic urethra. They are sometimes called the *excretory ducts* of the spermatogenic glands. They include the *straight tubules (tubuli recti)*, the cavernous spaces in the mediastinum *(rete testis)*, the ducts which convey the seminal fluid from the rete to the duct of the epididymis or the *efferent ducts (ductuli efferentes)*, and a long tubule. This latter is more or less arbitrarily divided into the *duct of the epididymis (ductus epididymis)*, the *ductus* or *vas deferens* and the *ejaculatory duct (ductus ejaculatorius)*.

THE STRAIGHT TUBULES. The straight tubules (tubuli recti) are short ducts formed by the union of the seminiferous tubules in the narrow portions of the lobules, and they connect the seminiferous tubules with the rete testis. Some of the straight tubules may be found in the septula. The epithelium of the seminiferous tubules undergoes a radical change as it approaches the tubuli recti; the spermatogenic cells disappear, the Sertoli cells remain as simple columnar elements which assume a cuboidal or flattened form in the straight tubules.

THE RETE TESTIS. The rete testis consists of a number of irregular spaces which, by their anastomoses, form an extensive network in the mediastinum. Some of the spaces are in the form of narrow clefts while others are widely distended. They are lined by low cuboidal

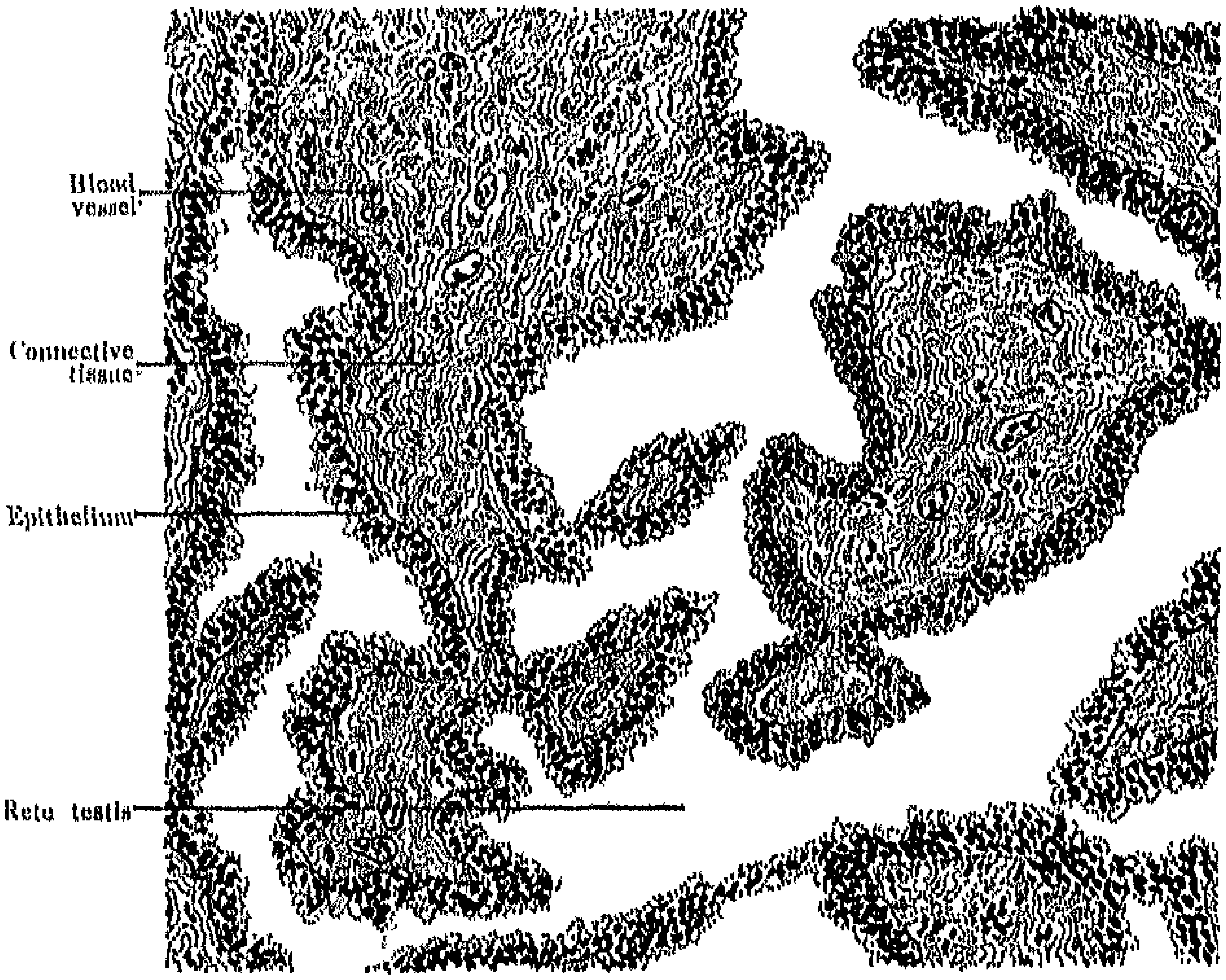


FIG. 226. Rete testis (human).

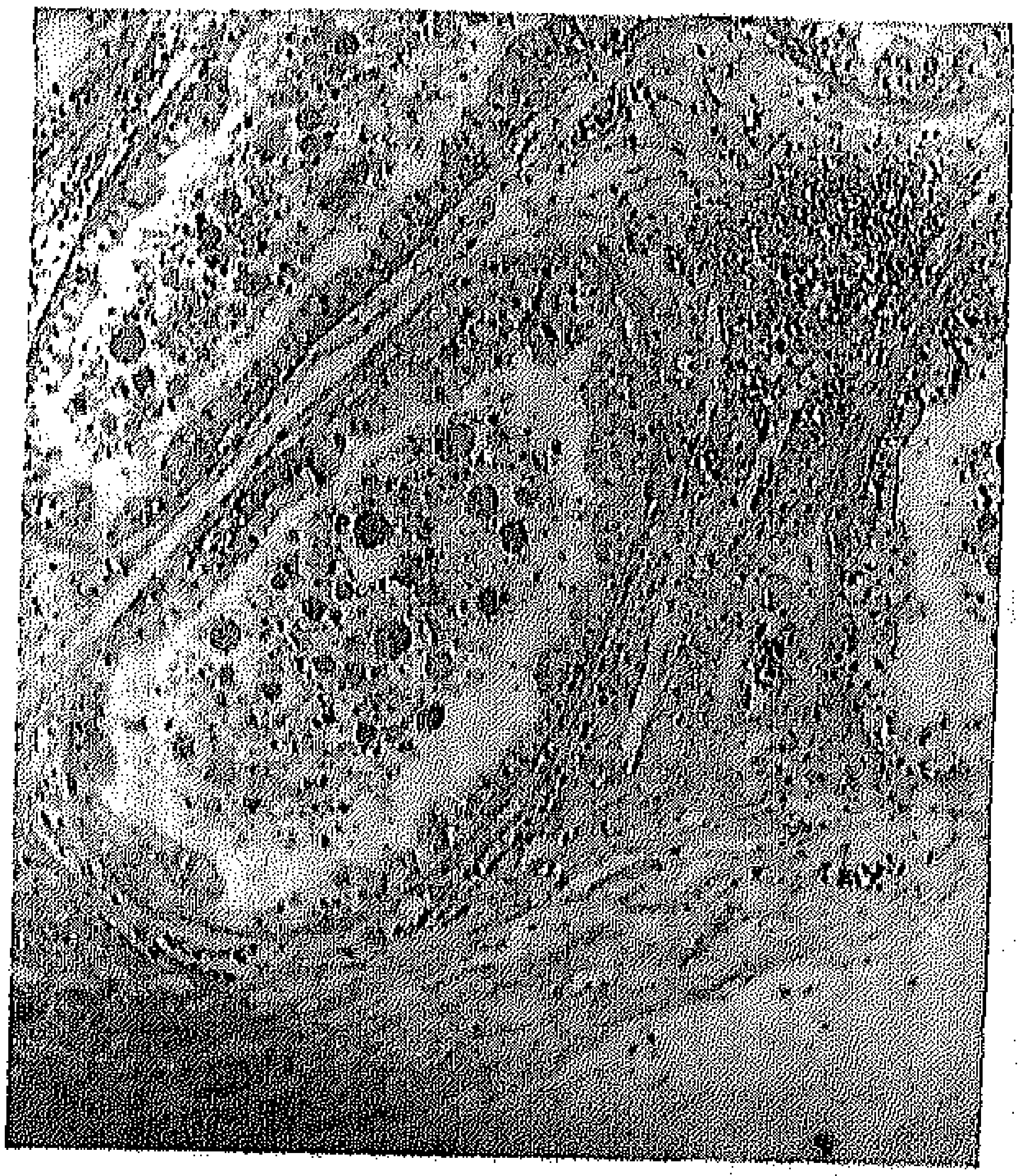
or flattened cells. No basement membrane is present, the epithelial cells resting directly on the fibrous tissue of the mediastinum. No muscle fibers are found in the tissue immediately surrounding the rete testis.

THE EFFERENT DUCTS. The efferent ducts connect the rete testis with the duct of the epididymis. They are lined by a simple type of epithelium made up of alternating patches of tall columnar and cuboidal cells. The difference in height of the two types of cells gives the epithelial lining of the efferent ducts a wavy appearance when seen in section. The cuboidal cells are secretory cells which are arranged in the form of small glandular invaginations. Because of this arrangement they are referred to as intraepithelial glands. The cells produce a secretion which frequently is observed adhering to the cilia in the form of droplets. The tall columnar cells likewise have cilia that beat in the direction of the duct of the epididymis. In their cytoplasm are found droplets of fat and pigment granules.

The epithelium of the efferent ducts rests on a thin basement membrane. External to the basement membrane is a thin layer of circularly directed smooth muscle fibers. The ducts are bound together and supported by loosely interwoven interstitial connective tissue, in which the nerve fibers and a few small ganglion cells of the *plexus myospermaticus* may be seen.

THE DUCTUS EPIDIDYMIS. The ductus epididymis is a single tubular structure, but is arranged in a number of coils, especially in the portion called the head (globus major). It is lined by a pseudostratified columnar epithelium, the basal row consisting of small cuboidal cells with deeply staining spherical nuclei while the superficial cells are tall and narrow with elongated nuclei which are located at different levels. The cytoplasm of these cells contains secretion granules, fat droplets and pigment granules. The free surfaces of the columnar cells are provided with cilia which adhere to one another and form a flame-shaped tuft. These cilia are nonmotile (stereocilia) and are related to the secretory processes of the cells. The secretion produced by the cells of the epididymis is believed to have an activating effect on the spermatozoa. External to the basement membrane the wall of the duct consists of a layer of circularly arranged smooth muscle fibers, which increases in thickness as the duct extends toward the vas deferens. The blood supply is by small vessels located in the surrounding connective tissue which form capillary networks about the wall of the duct. The nerves are the fibers and small ganglion cells of the plexus myospermaticus.

THE DUCTUS DEFERENS. The ductus deferens (vas deferens) continues from the lower end of the ductus epididymis to its junction with the duct of the seminal vesicle. It follows a winding course as it



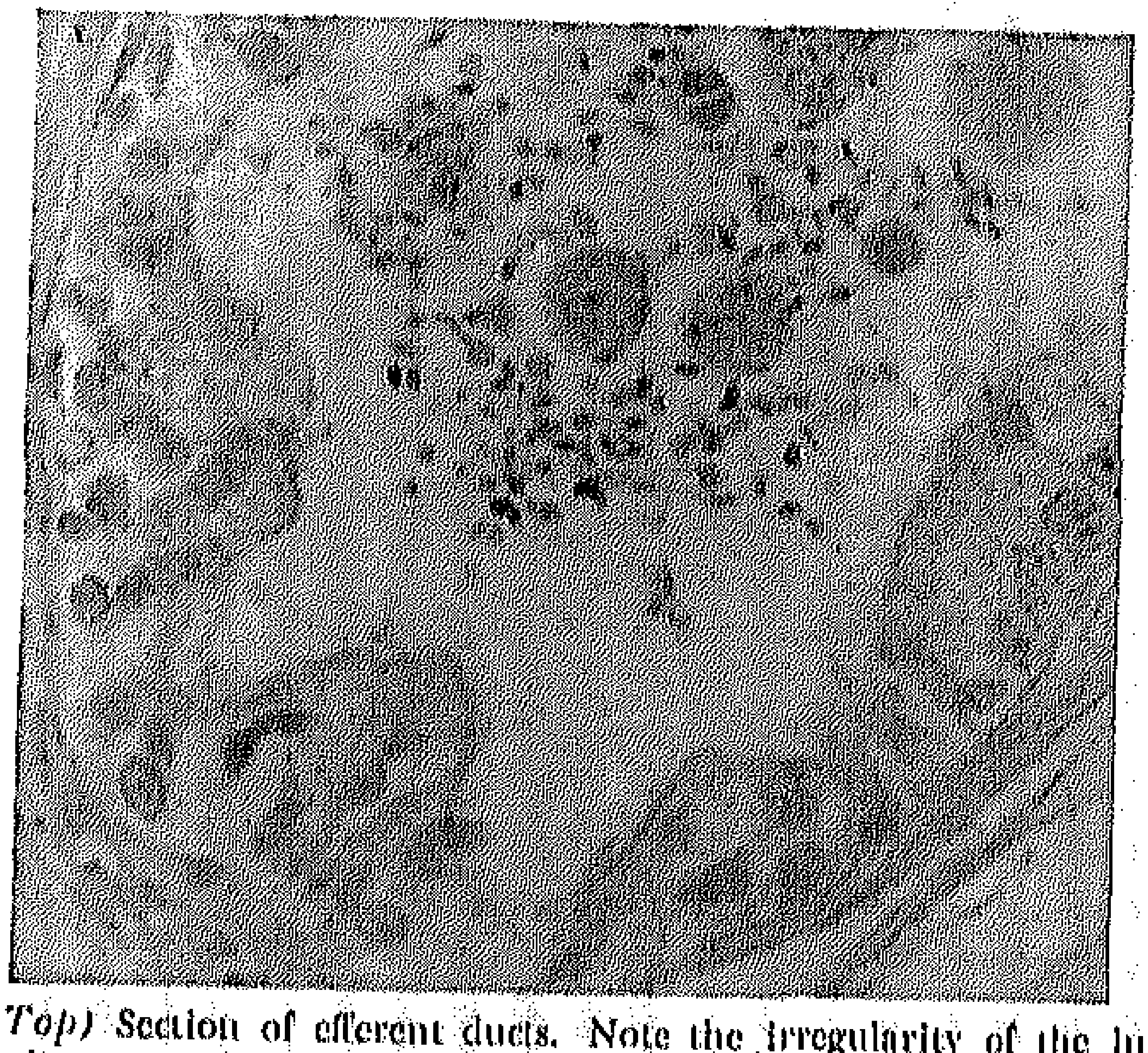


FIG. 227. *(Top)* Section of efferent ducts. Note the irregularity of the lumen due to areas of tall columnar cells interspersed with patches of low cuboidal cells. Photomicrograph.

FIG. 228. *(Bottom)* Portion of a section of an efferent duct showing detail of epithelium lining duct. High power magnification. Hematoxylin and eosin stain. Photomicrograph.

passes upward on the posterior surface of the epididymis, but straightens out as it enters the spermatic cord. Its upper end expands into a spindle-shaped enlargement, the *ampulla*. The wall of the ductus deferens consists of a *mucosa*, a *muscularis* and an *adventitia*, which is sometimes called the *fibrosa*. The mucosa includes an epithelium which rests on a thin basement membrane and an external subepithelial tissue or *stroma* made up of delicate, closely compacted connective tissue in which elastic fibers are abundantly present. This layer, which is really a stroma, is usually referred to as the tunica propria. In the proximal portion, the epithelium of the ductus deferens is a two-layered stratified columnar epithelium. In the distal portion, the basal layer of cells may be absent, the epithelium consisting of a single layer of columnar cells. Stereocilia may be present in some portions of the ductus deferens while absent in others. The muscularis consists of three layers of smooth muscle fibers. The small, scattered bundles of the inner layer are longitudinally directed. The middle layer of circular fibers is the best developed, while the outer longitudinal layer consists of scattered fiber bundles. The adventitia is formed by loosely

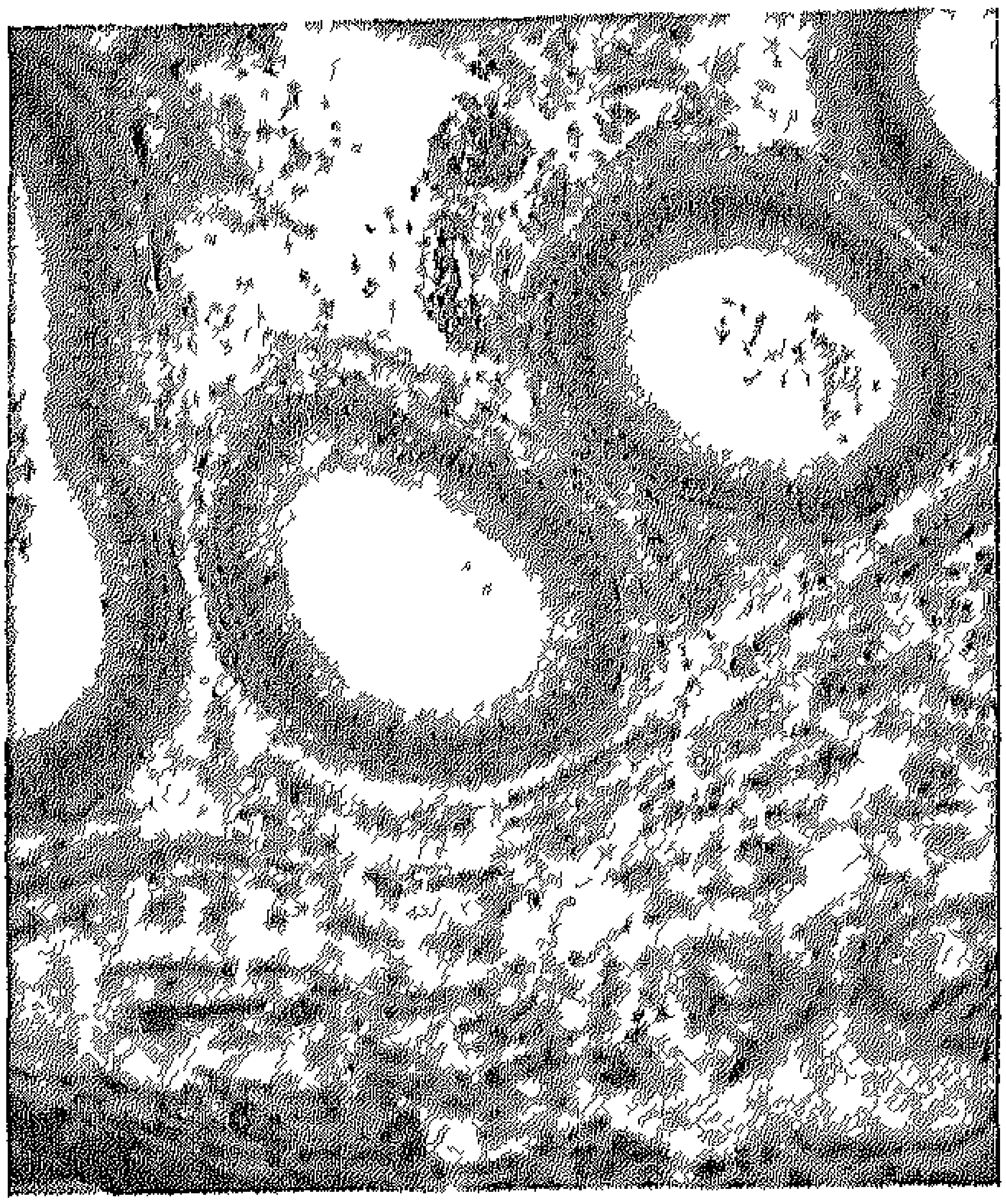


Fig. 229. Section through several ducts of the epididymis. Hematoxylin and eosin stain. Photomicrograph.

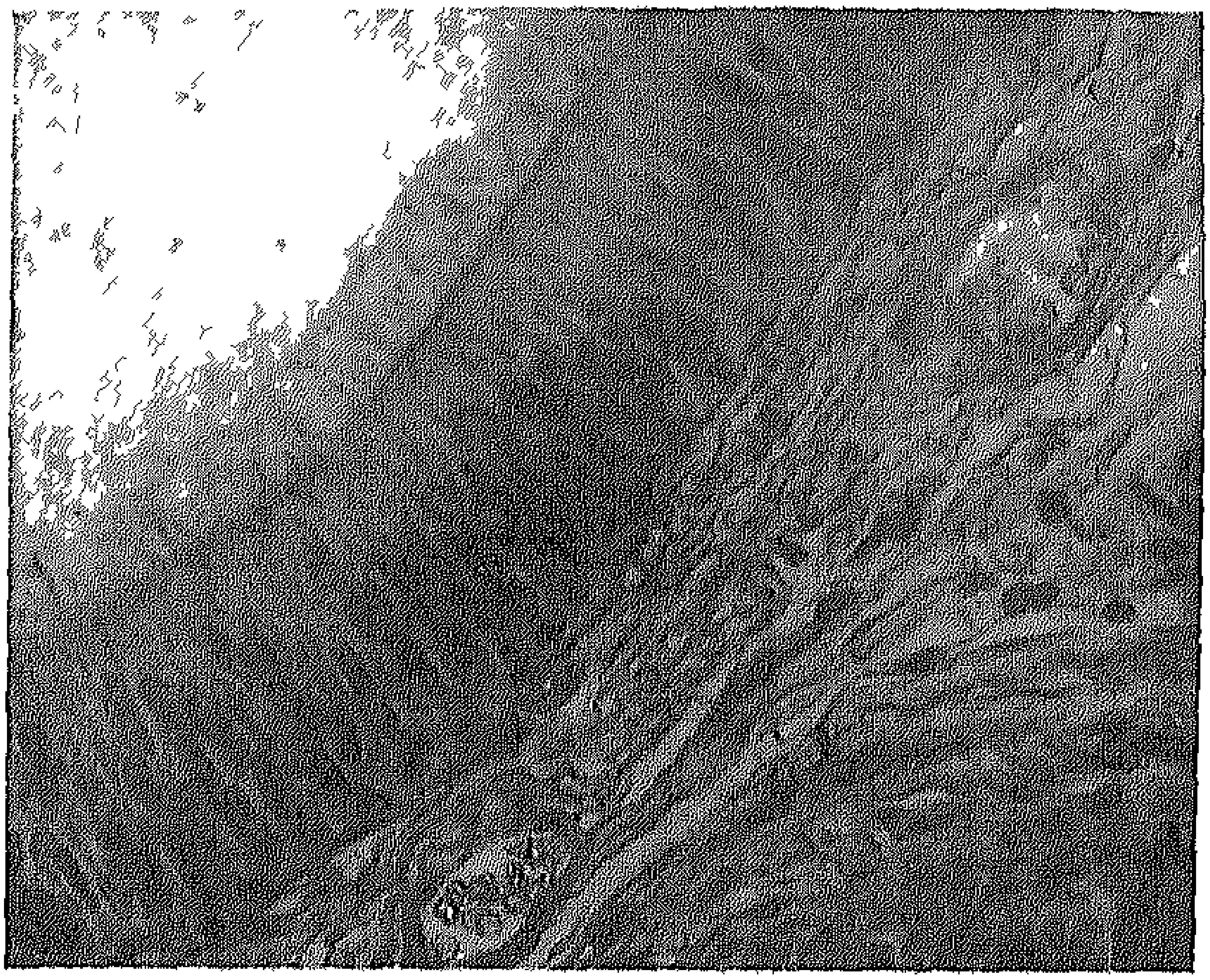


FIG. 290 Section through the ductus epididymis. Note the pseudostratified epithelium and the stereocilia Photomicrograph

arranged collagenous and elastic fibers which give support to the blood vessels and nerves, its connective tissue blending with that of the spermatic cord.

In the proximal end of the ductus deferens, the mucosa is raised into four or five broad, low folds, which give the lumen an irregular, star-shaped appearance. Toward the distal end the folds become taller and narrower. In the ampulla, secondary and tertiary folds are developed, some of which anastomose and enclose recesses or crypts.

THE EJACULATORY DUCTS. The ejaculatory ducts are formed by the union of the ductus deferens and the ducts of the seminal vesicles. The mucous membrane lining these ducts is similar in arrangement to that of the ampulla of the vas. The epithelium is simple columnar which changes to a transitional epithelium near the junction with the urethra. Immediately underlying the epithelium is a meshwork of elastic fibers. A muscularis is found only in the first part of the duct. As the duct penetrates the prostate, the dense fibromuscular wall of this gland supports the mucosa of the ejaculatory duct.

THE SPERMATIC CORD

The spermatic cord is a fibrous structure, extending from the internal inguinal canal into the scrotum where it is attached to the

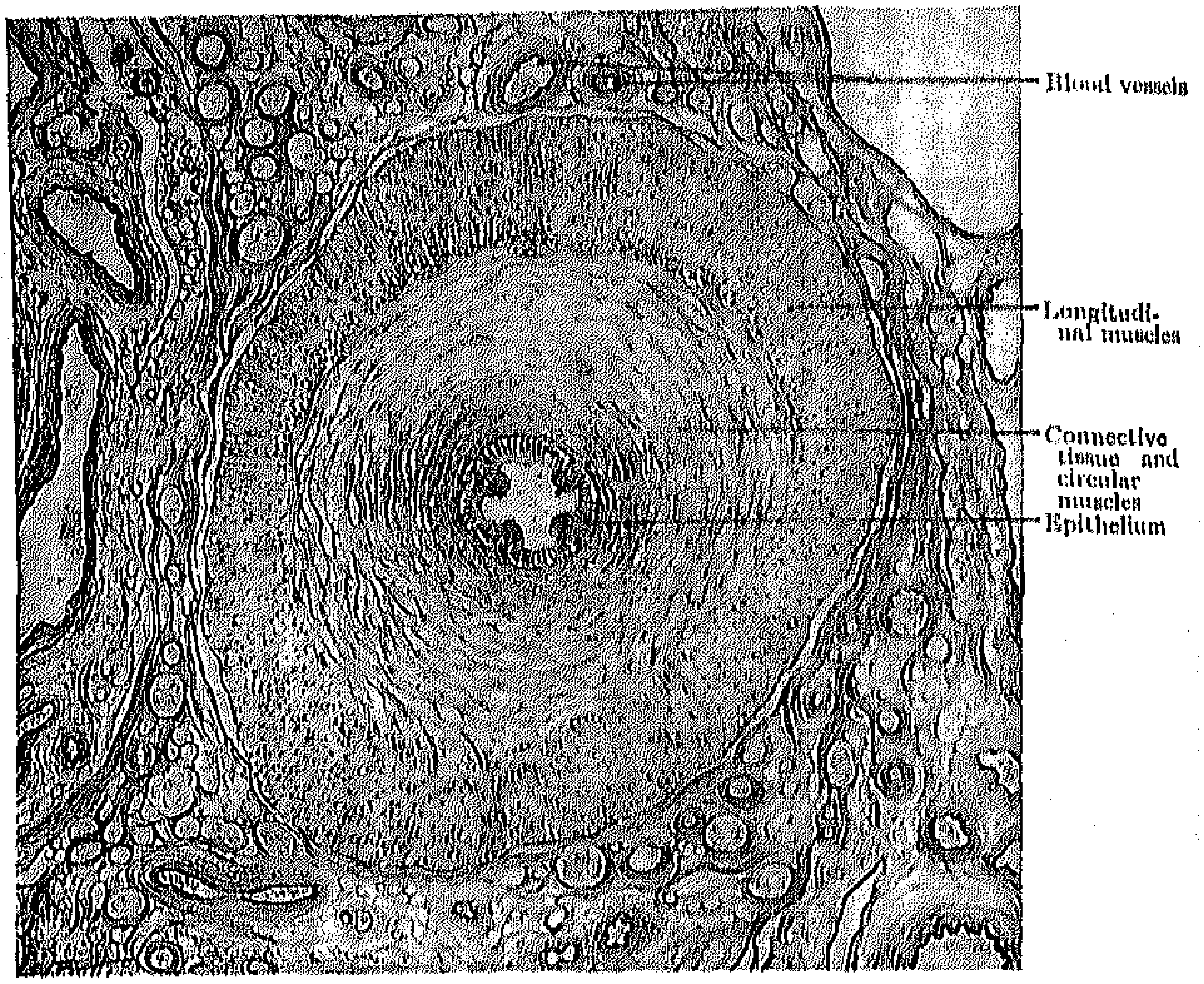


FIG. 231. Cross section through the ductus deferens (human). (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

posterior wall of the testis. In addition to the vas deferens, it contains the spermatic (testicular) arteries and nerves and a network of venous structures known as the *pampiniform plexus.* These structures are bound together by fibrous tissue and are enclosed by the fascial extensions of the abdominal wall which were carried by the testis in its descent into the scrotum.

GLANDS ACCESSORY TO THE GENITAL SYSTEM

The glands associated with the spermatic duct and which add their secretions to the seminal fluid, are the *seminal vesicles,* the *prostate gland* and the *bulbourethral glands.*

The Seminal Vesicles

The seminal vesicles are two elongated, irregularly shaped, saccular glands that are outgrowths from the vas deferens. Each vesicle consists of a number of diverticula bound together in a common capsule and opening into a common duct; they are usually referred to as *outpocketings.* The mucosa of these diverticula are raised into numerous tall ridges or folds, giving rise to secondary and tertiary folds which

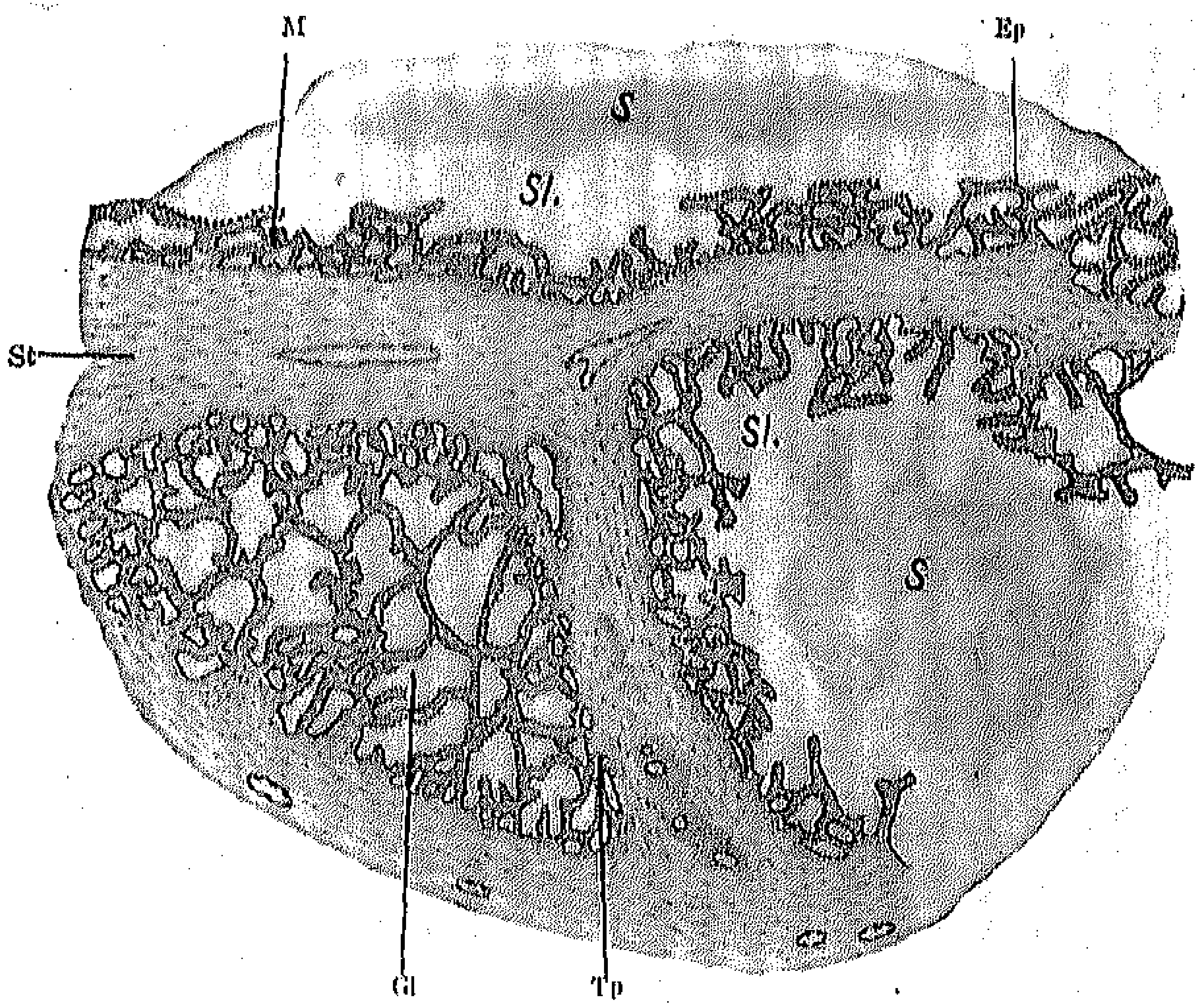


FIG. 282. Section through a sacculation and portions of two others of a seminal vesicle. (M) Mucous membrane, the ridges of which are united to form numerous crypts (alveolar surface). (Ep) Epithelium. (Sl.) Lumen. (Tp) Tunica propria. (Gl) Glandular crypts of the mucosa near an extremity of a sacculation. (St) Fibro-muscular stroma forming the walls of the sacculations. (S) Secretory material occupying the lumen.

unite and enclose recesses or crypts and give the surface a honeycombed appearance. Although some of the crypts are quite deep, they are continuous with the lumina of the diverticula. When seen in section, the crypts have the appearance of glands, although it is quite improbable that they have any special glandular function. These branching and anastomosing folds form that type of structure known as an *alveolar surface.*

The cells of the epithelium are usually described as cylindrical, varying in height from low to high columnar. The cytoplasm contains secretory granules, fat, and pigment, which appears at puberty and becomes more abundant with age. The granules are very refractive and stain with iron hematoxylin. They are soluble in acetic acid. The nuclei of these cells are large and round or oval with a distinct nuclear membrane and one or more nucleoli. The secretion produced in the seminal vesicles is a clear, alkaline, slightly sticky fluid which forms a major portion of the seminal fluid. It coagulates into a stringy mass when acted upon by certain reagents. No special function is known,

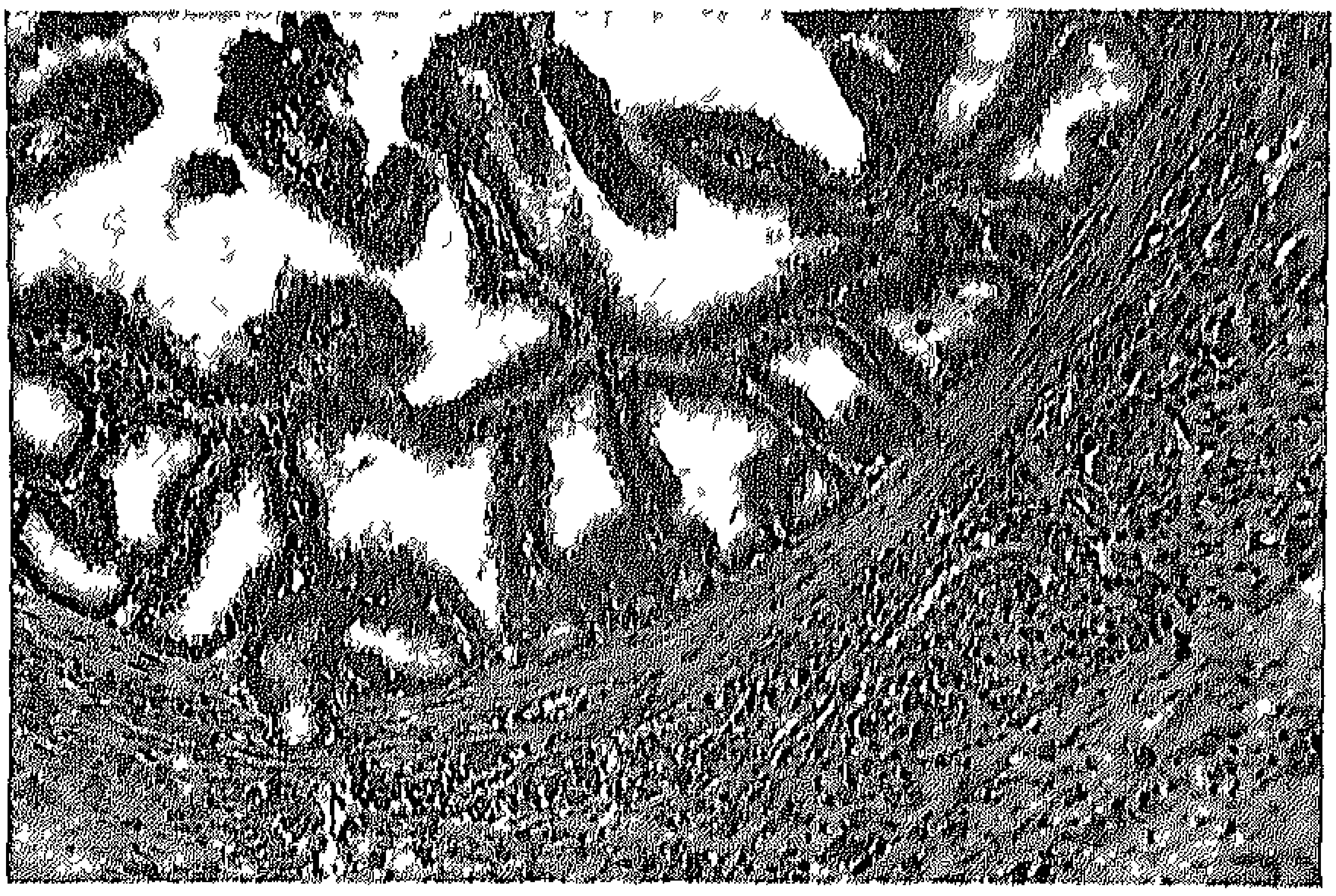


FIG. 233. Section through a portion of the wall of the seminal vesicle. Hematoxylin and *eosin stain. Photomicrograph*

but (in some animals) it forms a vaginal plug for the retention of the sperm in the uterus.

The epithelium rests directly on the underlying tissue. There is no basement membrane. The tissue which lies external to the epithelium consists mostly of elastic fibers, although a few collagenous fibers are present. This stroma is enclosed by a thin layer of smooth muscle fibers which are circularly arranged for the most part. Outside of the muscular coat, the wall consists of a layer of fibroelastic tissue supporting the blood vessels and nerves by which the vesicles are supplied.

THE PROSTATE GLAND

The prostate gland is a triangular body about the shape and size of a chestnut. It lies with its base applied to the inferior surface of the bladder, its apex being directed downward. The prostatic portion of the urethra extends the entire length of the gland and the ejaculatory ducts penetrate the wall of the prostate gland to join the prostatic portion of the urethra.

The prostate is enveloped by a capsule of fibroelastic tissue, the inner layer of which contains small bundles of smooth muscle fibers. Its framework consists of fibrous tissue which extends into it from the capsule. This includes a broad, median septum, extending dorsally from the ventral surface, and a number of septa, consisting of fibroelastic and muscular tissue, which reach from the median septum to

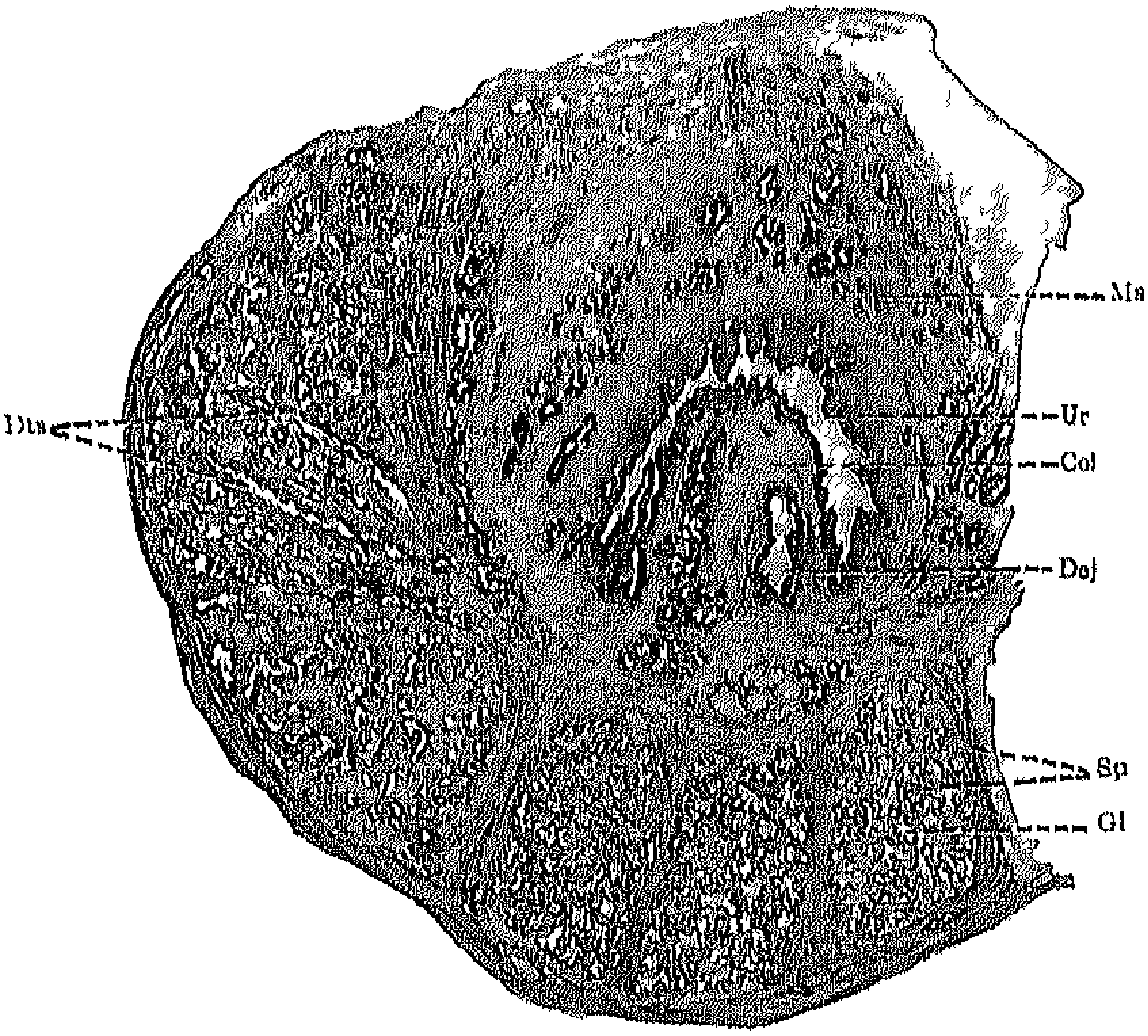


Fig. 284. Prostate gland. (Ms) Medium septum. (Ur) Prostatic urethra. (Col) Colliculus seminalis (crista urethralis). (Dej) Ejaculatory duct. (Sp) Septal connective tissue. (Gl) Lobules of glandular tissue. (Dis) Lobular ducts

the capsule. These septa divide the gland into a number of compartments or lobules, in which the glandular tissue is located. The median septum encloses the prostatic portion of the urethra.

The smooth muscle fibers which are present in the capsule are continued into the septa, and constitute about one-fourth of the substance of the gland with the connective tissue comprising another fourth. A little more than half of the prostate consists of glandular tissue.

The prostate gland is made up of a number of branched tubulo-alveolar glands with their accompanying ducts. From 15 to 20 lobular ducts open into the urethra. These ducts, as they pass outward into the lobules, divide repeatedly, their branches ending in expanded tubules or *alveoli.* The alveoli are lined by a simple columnar or cuboidal epithelium, the cells of which rest on a thin layer of fibrous tissue. Basal cells may be present. The cytoplasm of these alveolar cells contains secretory granules and fat droplets. The nuclei are clearly defined and are oval in shape and vesicular. The secretion is a slightly alkaline fluid, having a milky appearance and a characteristic

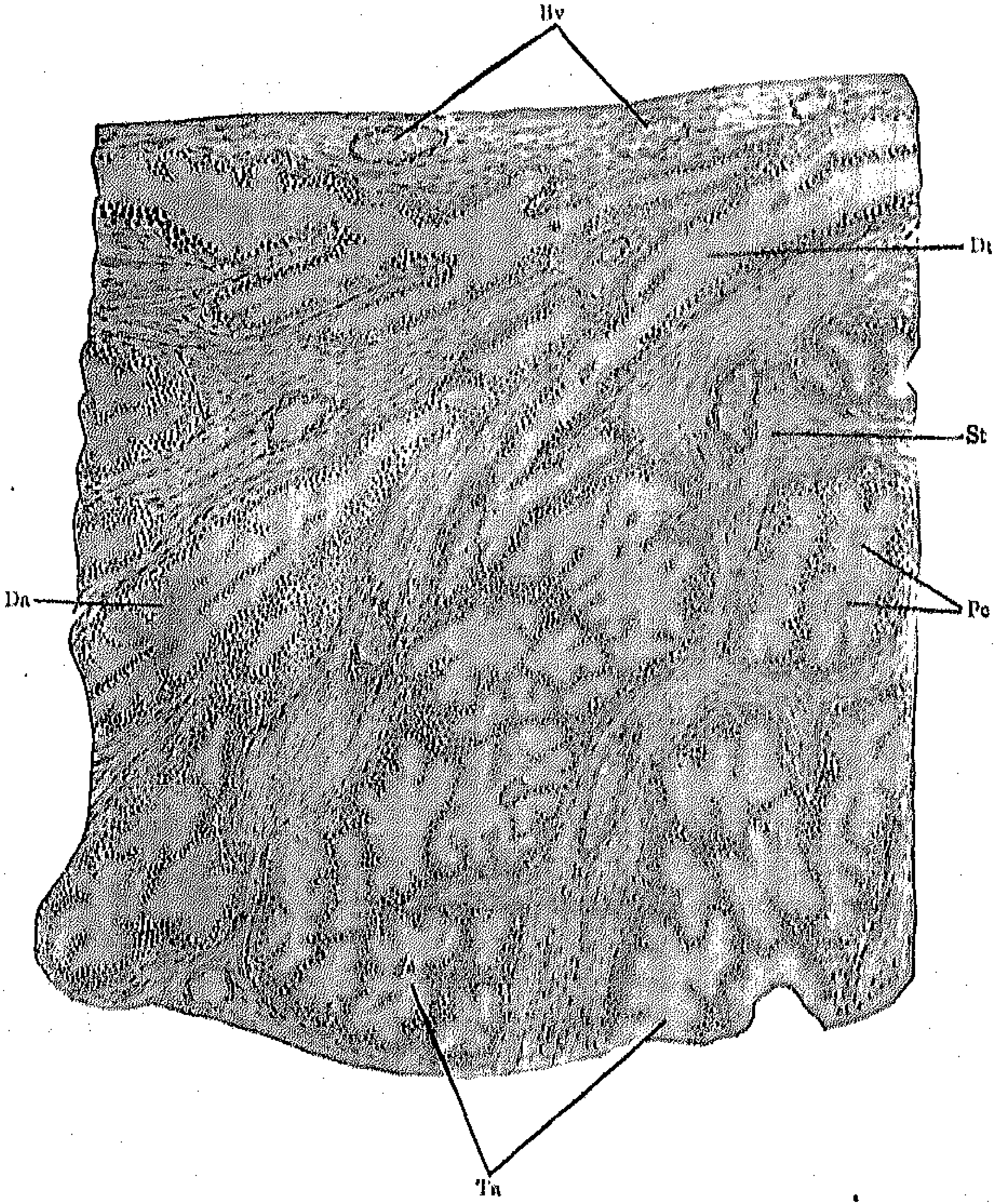


FIG. 285. Section through the prostate gland. (Dt) Prostatic duct. (St) Fibro-muscular stroma. (Da) Duct alveoli. (Ta) Terminal alveoli. (Pc) Prostatic concretion. (Bv) Blood vessels.

odor. It exerts a stimulatory influence on the motility of the spermatozoa, alkalizes the acidity of the vagina and coagulates the fluid of the seminal vesicles.

The alveoli appear to be quite irregular in form. This is due to the folds of varying height into which their walls are raised. The epithelium frequently appears to be two-layered, especially where it passes over the taller folds (a surface layer of columnar cells and a basal layer of cuboidal cells). Saccular and tubular diverticula occur

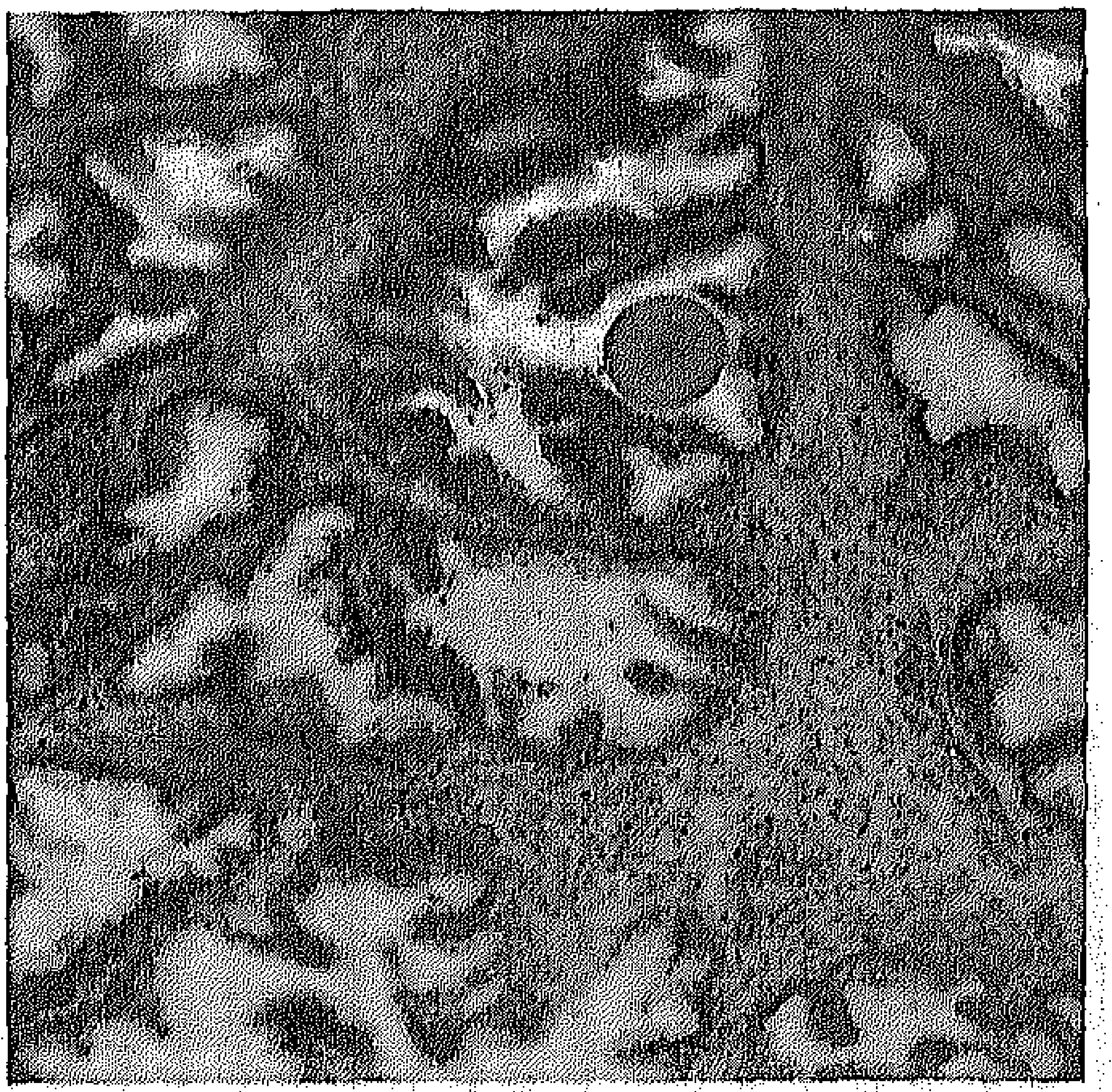


FIG. 236. Section of prostate gland. Note the corpus amylaceus in the lumen of one of the alveoli. Hematoxylin and eosin stain. Photomicrograph.

long the course of the ducts. These diverticula are known as the *duct alveoli*, in contrast to the branched and expanded structures in which the ducts end, the *terminal alveoli*. The lobular ducts are lined by a simple columnar epithelium which continues almost to their junction with the urethra, where it changes to the transitional form.

The larger and more expanded alveoli, especially in the prostates of older people, contain round or oval bodies called *prostatic concretions (prostatic calculi)*. These concretions are light brown in color and are formed in concentric layers, the outlines of which are faintly visible. Their starchy nature is indicated by their reaction to iodine and they are sometimes called *amyloid bodies (corpora amylacea)*.

The *colliculus seminalis (crista urethrae)* is formed by a thickening of the prostatic tissue which constitutes the dorsal wall of the urethra and into which it extends as a mound-shaped elevation. This elevation is covered by a continuation of the transitional epithelium which lines the urethra, except on its sides where extensions of the urethra form deep furrows known as the prostatic sinuses. The prostatic sinuses are lined by a stratified columnar epithelium. The epithelial cells rest on a substratum or *stroma* (sometimes referred to as a tunica propria) of connective tissue. This tissue is richly supplied with elastic fibers and is continuous with that of the median septum.

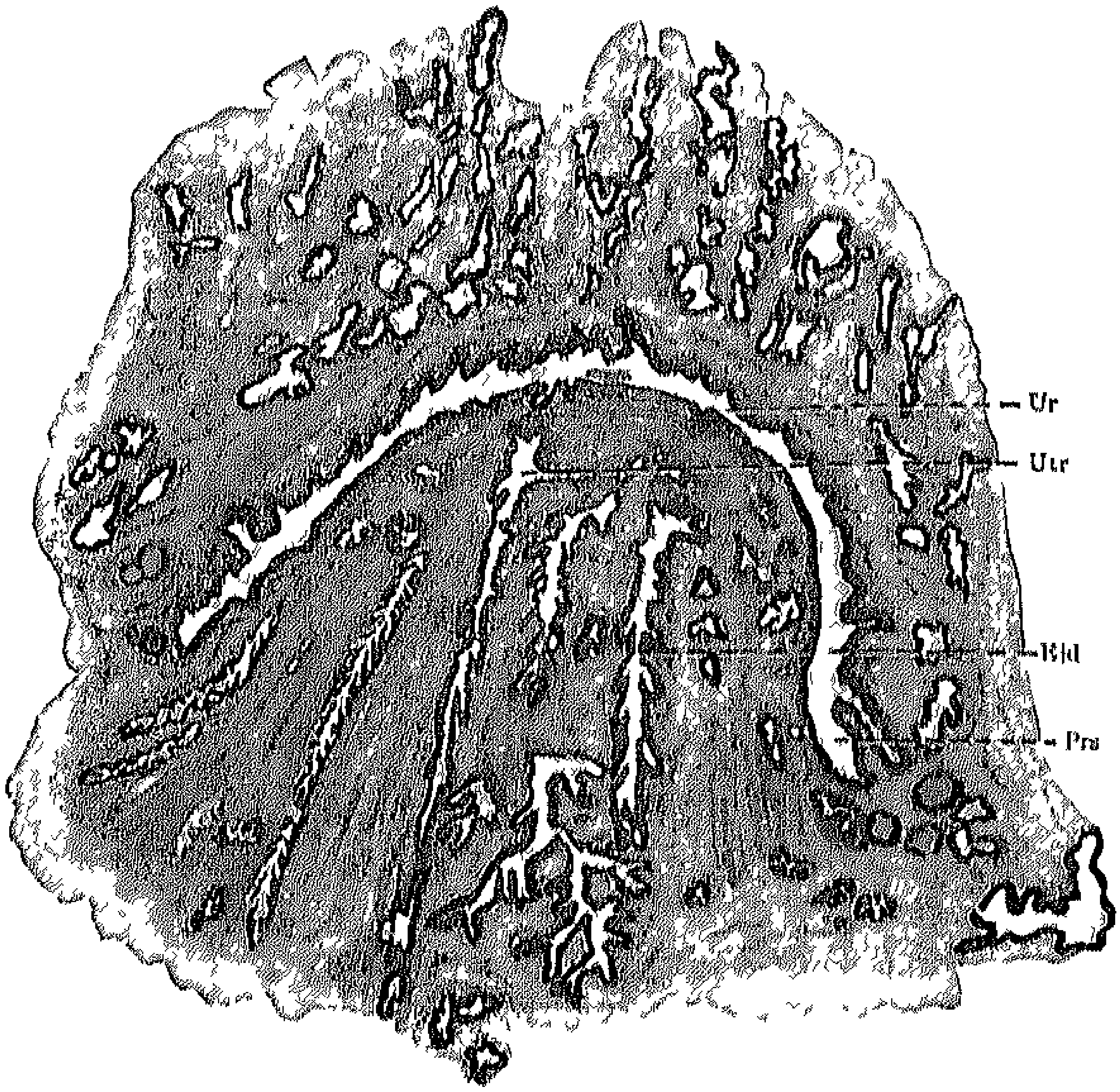


FIG. 287. The prostatic urethra showing the relation of the urethra to the colliculus seminalis (crista urethralis). (Ur) Prostatic urethra. (Utr) Utriculus. (Ejd) Ejaculatory duct. (Prs) Prostatic (urethral) sinus.

At the summit of the colliculus, a small, slitlike opening leads into a tubular structure, the *utriculus prostaticus (uterus masculinus)*, which represents the lower end of the Müllerian duct. The utriculus is lined by a simple columnar epithelium and may extend for some distance in the dorsal direction in the gland. The *ejaculatory ducts*, which are lined by a transitional epithelium as they pass through the colliculus, open into the urethra on either side of the utriculus. Portions of the glandular tissue of the prostate are also present in the fibrous tissue of the colliculus. Blood vessels which enter with the ejaculatory ducts, form a plexus of thin-walled capillary structures, giving the colliculus the appearance of being supported by erectile tissue.

The blood vessels supplying the prostate enter the capsule at various points, their branches passing into the gland in the septa. Small branches from the vessels in the septa extend into the lobules, where they break up into capillaries which form networks about the alveoli. The veins take their origin from the capillaries, and passing into the septa, accompany the arteries to the capsule, where they form an extensive network, the branches of which convey the blood from the gland.

The lymphatics arise in the connective tissue of the lobules and follow the course of the arteries to the surface of the gland.

The nerves are mainly unmyelinated fibers from the autonomic system. Some of these fibers come into association with small ganglion cells in the capsule and septa. Postganglionic fibers pass to the walls of the blood vessels, the bundles of smooth muscle fibers and, probably, to the walls of the alveoli. Sensory fibers also enter the gland and end in relation to special sensory structures in the capsule.

THE BULBOURETHRAL GLANDS

The *bulbourethral (Cowper's) glands* are located close to the membranous urethra. They are about the size and shape of a pea, although they often present marked irregularities of form. They communicate by ducts of considerable length with that portion of the urethra which is located in the bulb of the corpus spongiosum. The glands are of the compound tubuloacinar (alveolar) type, that is, they may end in rounded sacs or elongated tubules. The glandular tissue is divided into small lobules by fibrous septa which are continuations from the capsule, and like the capsule, consist of collagenous and elastic tissue. Both smooth and striated muscle fibers are present. The striated fibers are derived from the deep perineal muscles. The cells with which the secreting portions of the glands are lined are, as a rule, pyramidal in form. However, they may be low columnar or cuboidal, the shape and size of the cells varying with the degree of their functional activity. In acini which are distended by an excess of secretory material, the cells may be decidedly flattened. The nuclei are located in the basal portions of the cells. The cells have the appearance of being filled with a mucoid substance and in addition they contain bodies which stain with the acid dyes. The secretion of the glands is a clear, viscid fluid with a strong alkaline reaction and it aids in neutralizing the acidity of the vagina.

The smaller ducts are lined by a cuboidal epithelium and have outpocketings which resemble the secretory portions of the glands. The larger ducts are lined by a simple columnar epithelium, while near their outlets the epithelium is of the stratified columnar type.

THE PENIS

The penis is an elongated organ consisting of three cylindrical bodies: the two *corpora cavernosa* are dorsal in position and the third, the *corpus spongiosum (corpus cavernosum urethrae)*, is ventrally placed. Each of these bodies is enveloped by a thick (1 mm.) sheath of densely compacted fibrous tissue, the *tunica albuginea*, the fibers being longitudinal in direction in its outer portion and circular in its inner portion. The portion of the tunica albuginea which is continued between the corpora cavernosa is called the *median septum*. The median septum is not as strongly developed as the other parts of the albuginea and in its anterior portion, is pierced by numerous apertures through which the blood spaces in the corpus cavernosum on one side can communicate with the spaces in the corpus cavernosum on the other side. The sheath about the corpus spongiosum is thinner and more elastic than that about the corpora cavernosa. The corpus spongiosum encloses the penile portion of the urethra, which extends its entire length. It ends in a cone-shaped enlargement, the *glans penis*, in which the terminal portion of the urethra is expanded to form the *fossa navicularis*.

The *body* or *shaft* of the penis is covered by a thin layer of skin. The subcutaneous tissue between the skin and the tunica albuginea is relatively thick and contains a considerable amount of smooth muscle, resembling in this respect, the dartos of the scrotum. Except at its base, the penis is devoid of hair, although a few sweat and sebaceous glands are present. The skin turns over the glans in the form of a fold which is called the *prepuce*. The under surface of this fold is supplied with a number of modified sebaceous glands, the *glands of Tyson*. The skin over the glans is deeply papillated.

Connective tissue extends from the tunica albuginea into the corpora cavernosa and corpus spongiosum, forming the narrow trabeculae between which are large venous blood spaces called *lacunae*. The trabeculae and lacunae together constitute the erectile tissue of the penis. Besides the fibroelastic tissue of which they are composed, the trabeculae are well supplied with smooth muscle fibers. The walls of the blood spaces consist of a layer of thin endothelial cells which lie directly on the fibro-muscular tissue of the trabeculae.

The lacunae, in the central portion of the corpora cavernosa, are larger and the trabeculae thinner than in the peripheral portion. In the flaccid condition of the organ, the lacunae are collapsed and appear as narrow, irregular slits in a stroma of connective tissue.

The erectile tissue in the corpus spongiosum consists of small lacunae between relatively thick trabeculae and is continuous with the venous plexus in the mucosa of the urethra.

The penis is supplied with blood by the two branches of the penile artery. The superficial branch, the *arteria dorsalis*, lying in the connective tissue above the corpora cavernosa, is accompanied by the dorsal veins. The divisions of the deep branch, *arteria profunda*, run lengthwise in the corpora cavernosa.

The flow of blood through the penis depends on whether it is in a flaccid or rigid condition. Branches from the dorsal artery extend to the albuginea, where they form a network from which branches pass into the larger trabeculae of the corpora cavernosa. These branches communicate through intervening capillaries with the central lacunae. From the central lacunae the blood passes through small veins to the peripheral lacunae, which are smaller than the central ones, and finally by venous branches to the plexus in the albuginea. This ultimately communicates with the deep veins of the penis which convey the blood from the organ.

The deep arteries, which furnish most of the blood to the corpora cavernosa, send many branches into the trabeculae between the central lacunae. The muscular portion of the wall *(media)* of these vessels is very thick. Their length is such that when the tissues of the penis are relaxed, they are coiled about in such a way that they frequently project into the lacunae. These vessels are known as the *helicine arteries.* The intima of the helicine arteries is thickened by bundles of longitudinal smooth muscle fibers which form cushionlike pads that project into the lumina of the vessels. When the arteries are contracted, this pad serves as a plug and allows only a small trickle of blood to pass through into the central lacunae. From these lacunae it is borne by small vessels into the peripheral lacunae, through which it flows into the venous plexus in the tunica albuginea. During erection the helicine arteries are straightened and relaxed, the blood flowing through them freely into the central lacunae, which become distended by the increased pressure of the added supply of blood. These distended central lacunae press upon the smaller peripheral lacunae, thus checking, or at least reducing, the flow of blood into the venous plexus of the albuginea. Some drainage of the central lacunae is effected by a series of special veins with funnel-shaped valves which open directly from their walls. However, the flow of blood out of the lacunae is impeded to the extent that the organ attains a condition of extreme rigidity.

The penis returns to the flaccid condition by the contraction of the helicine arteries. This shuts off the increased flow of blood from the deep arteries to the central lacunae and permits the special veins to empty them. The pressure on the smaller peripheral lacunae is soon reduced and the flow of blood through them is reëstablished. The emptying of the lacunae is aided by the smooth muscle fibers in the trabeculae, which are able to contract effectively as soon as the excess pressure of the dilated lacunae is removed.

The corpus spongiosum does not attain the same degree of rigidity during erection as the corpora cavernosa, due to the greater elasticity of its connective tissue, the thickness of its trabeculae, and to the fact

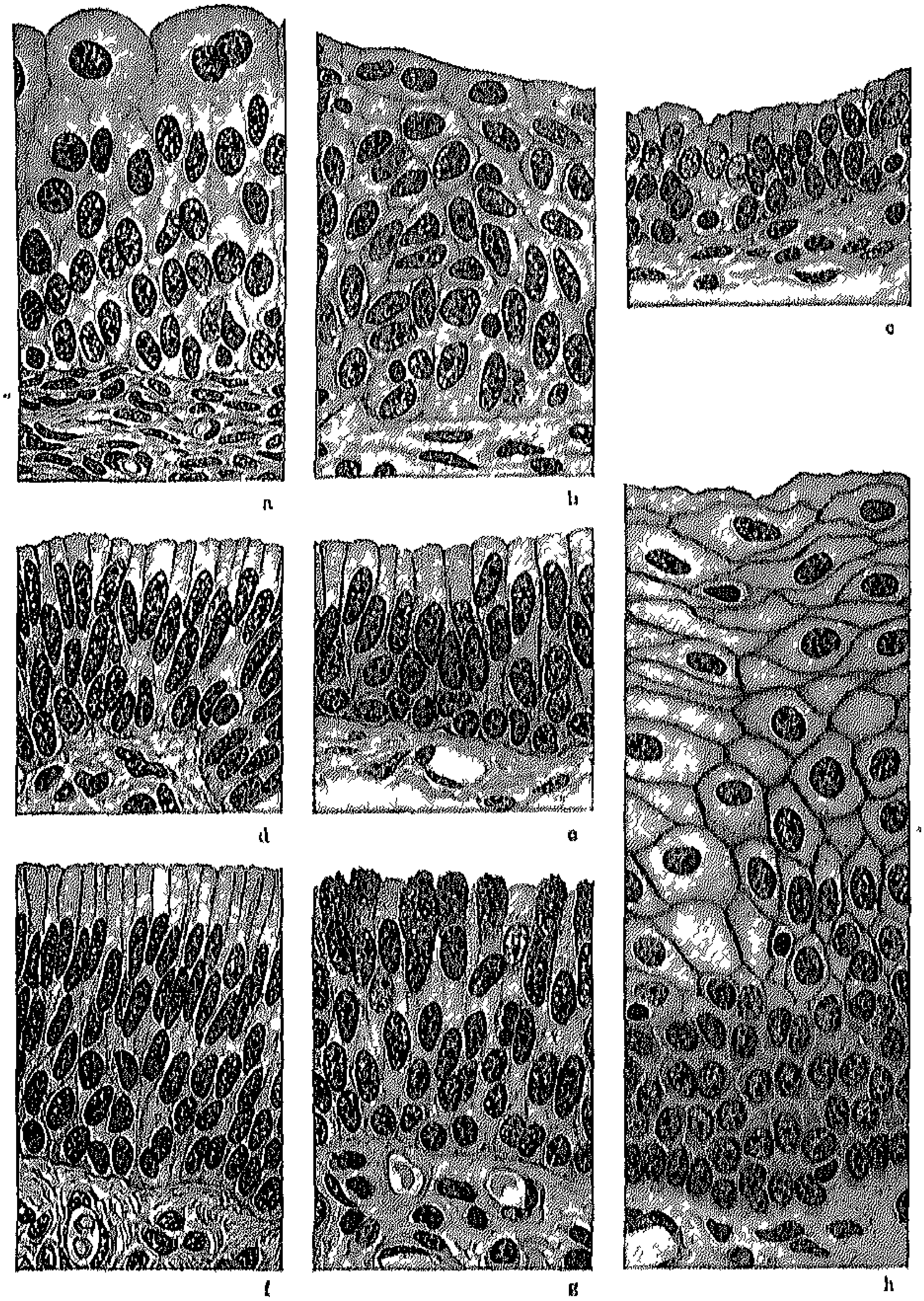


FIG. 298. Sections from different parts of the male urethra showing changes in the character of the epithelium. (a) Near the bladder. (b) Inner portion of prostatic part. (c) Outer *portion of prostatic part. (d) Diaphragmatic part. (e) Ampulla (f) Middle of cavernous part.* (g) Inner part of fossa navicularis showing goblet cells. (h) Outer part of fossa navicularis. (After Stieve) (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

that the peripheral lacunae are as large as the central ones. Less obstruction to the flow of blood is thus offered.

The lymphatics arise from capillaries in the trabeculae of the erectile tissue, the mucosa of the urethra and in the skin. They drain into nearby lymph nodes.

The nerves are from both the spinal and autonomic centers. The autonomic fibers are distributed to the walls of the blood vessels and to the smooth muscle fibers in the erectile tissue. The sensory fibers are from the spinal nerves and end in special sense organs in the dermal papillae *(Meissner's corpuscles)* and in the deeper portions of the subdermal connective tissue *(Pacinian corpuscles; end bulbs of Krause; genital corpuscles)*. Fibers from the third and fourth sacral nerves, the *nervi erigentes*, pass with the autonomic fibers to the erectile tissue and are related to the act of erection, because the latter does not occur when these nerves are cut.

THE URETHRA

The male urethra presents three divisions: the *prostatic*, the *membranous*, and *penile* divisions. The penile division is sometimes referred to as the "spongy urethra." The prostatic division has already been described (see colliculus seminalis, p. 407). The membranous urethra is a short segment extending from the apex of the prostate gland to the urethral bulb of the corpus spongiosum. Its wall consists of a stratified columnar epithelium resting on a thin, subepithelial stroma. The muscular coats external to the stroma consist of a thin layer of longitudinally directed smooth muscle fibers and a thicker outer layer of circular, smooth muscle fibers.

The epithelium of the penile urethra remains stratified columnar until it changes to the stratified squamous form in the fossa navicularis, the epithelial lining of which is continuous with the integument of the glans penis.

About the outlet of the bladder the muscular coat is a relatively thick layer of circular fibers. From here it gradually diminishes in thickness until it begins to disappear a short distance beyond the membranous urethra, first from the lower part and then from the upper part of the urethral wall. As the fibers of the intrinsic muscular coat diminishes, their place is taken by the smooth muscle fibers of the surrounding spongy tissue.

The urethra gives rise to a number of glandular structures known as the urethral *glands of Littré*. These are of two kinds: the *short glands*, which are saccular outpocketings of the urethral wall, and the *long glands*. The short glands occur along the entire length of the urethra and are lined by a columnar epithelium. The long glands are provided with ducts which extend for some distance posteriorly, their course being parallel with that of the urethra. These ducts end in a number of branched tubular alveoli which are lined by a simple columnar epithelium. The epithelium of the urethra frequently forms tubular, nonglandular depressions, the ***urethral crypts***, into which the ducts of the glands of Littré open.

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The Female Reproductive Organs

The female reproductive organs are the *ovaries*, the *oviducts (uterine* or *Fallopian tubes)*, the *uterus*, and the *vagina*. The external genitalia consist of the two *labia (majora* and *minora)*, and the *clitoris*.

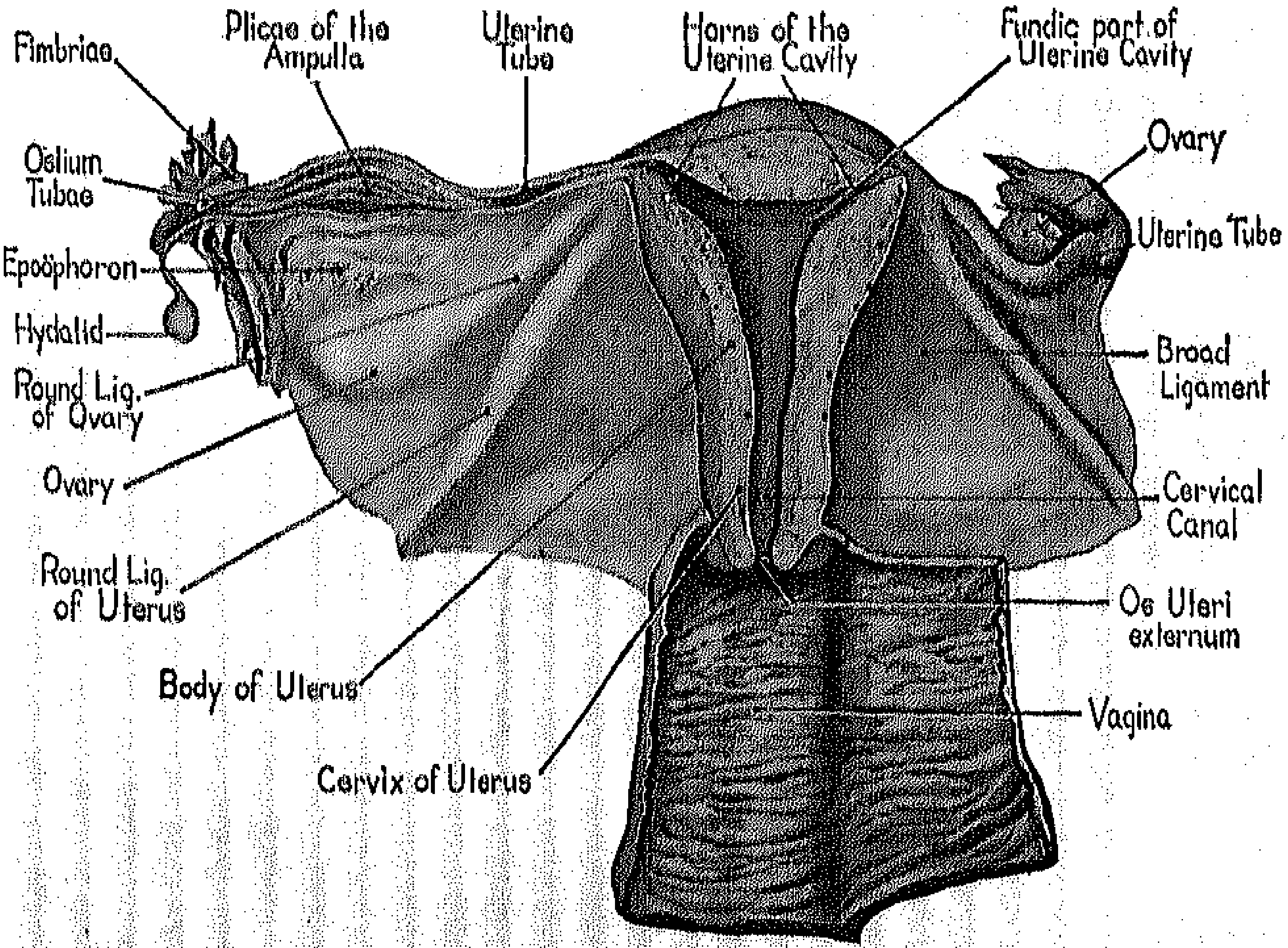


FIG. 239. Internal reproductive organs of the female spread out and viewed in ventral aspect. (Modified from Rauber-Kopsch: Lehrb. u. Atlas der Anat. des Menschen.) Vagina, uterus and right uterine tube have been opened to show their internal configuration. (Courtesy, Patten: "Human Embryology," Philadelphia, The Blakiston Company.)

The mammary glands are accessory organs of reproduction since their function is to nourish the newborn young, but since they are morphologically structures which are related to the skin they have been presented in that connection.

THE OVARIES

The ovaries are slightly flattened, ovoid bodies located on each side of the body in the lower abdominal cavity. The size of the ovaries varies somewhat in different individuals, however, on the average they are about 3 cm. long, 2 cm. wide, and 1 cm. thick. Each ovary is fastened to the broad ligament of the uterus by means of a fold of connective tissue known as the *mesovarium,* which attaches along the hilum and the border of the ovary. The mesothelial cells which form the external layer of the mesovarium end abruptly at the hilum and are succeeded by a layer of cuboidal cells which constitute the *germinal epithelium,* the layer that covers the surface of the ovary. The fibrous tissue of the broad ligament is continued through the mesovarium into the ovary in which it spreads out and forms the stroma of the medulla.

The ovary is divided into two zones: an outer portion, the *cortex (zona parenchymatosa)* and an inner portion, the *medulla (zona vasculosa).* The tissue of the cortex blends gradually into the tissue of the medullary portion.

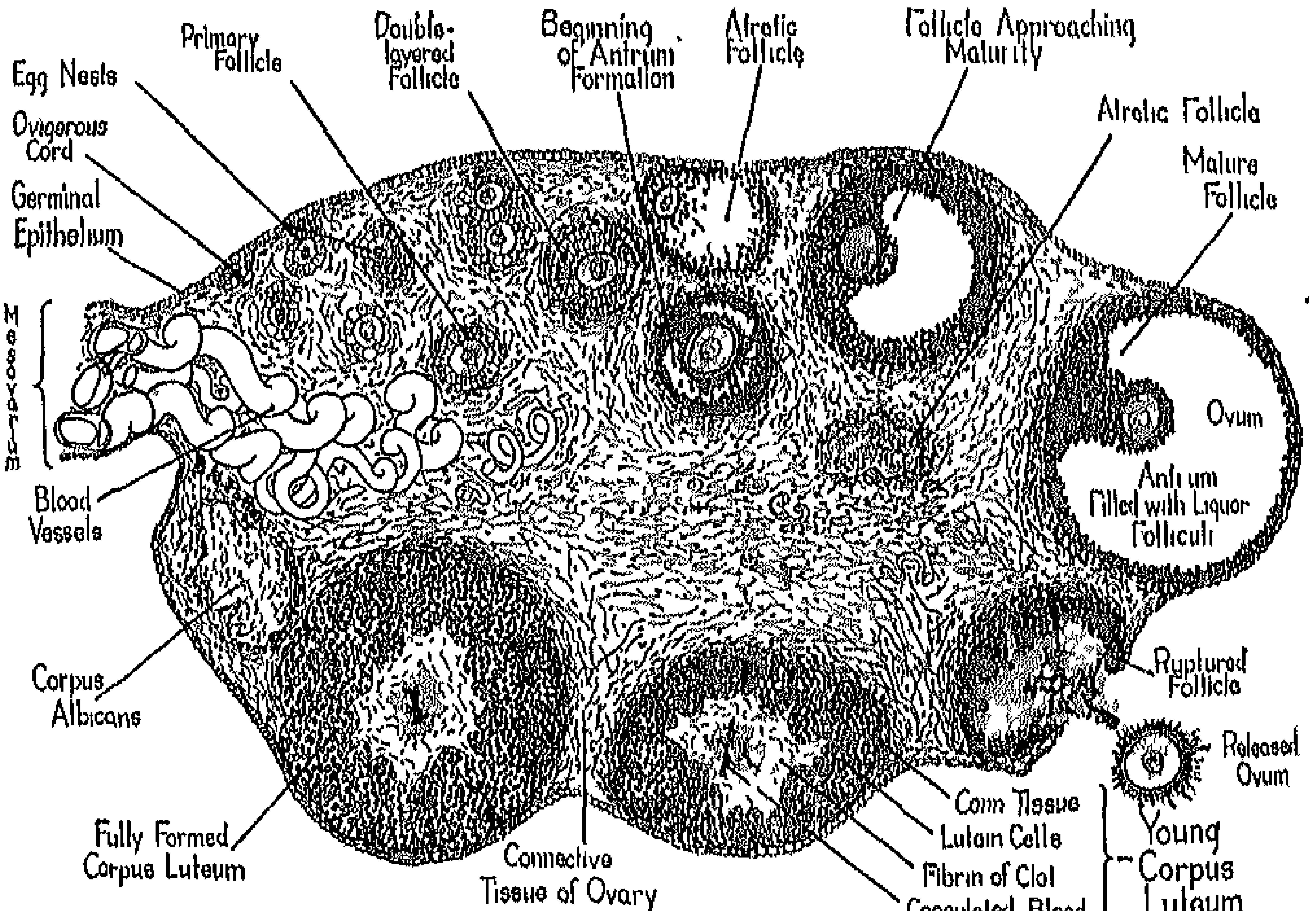


FIG. 240. Schematic diagram of ovary showing sequence of events in origin, growth, and rupture of ovarian (Graafian) follicle, and formation and retrogression of corpus luteum. *Follow clockwise around ovary, starting at mesovarium. (Courtesy, Patten:* "Human Embryology," Philadelphia, The Blakiston Company.)

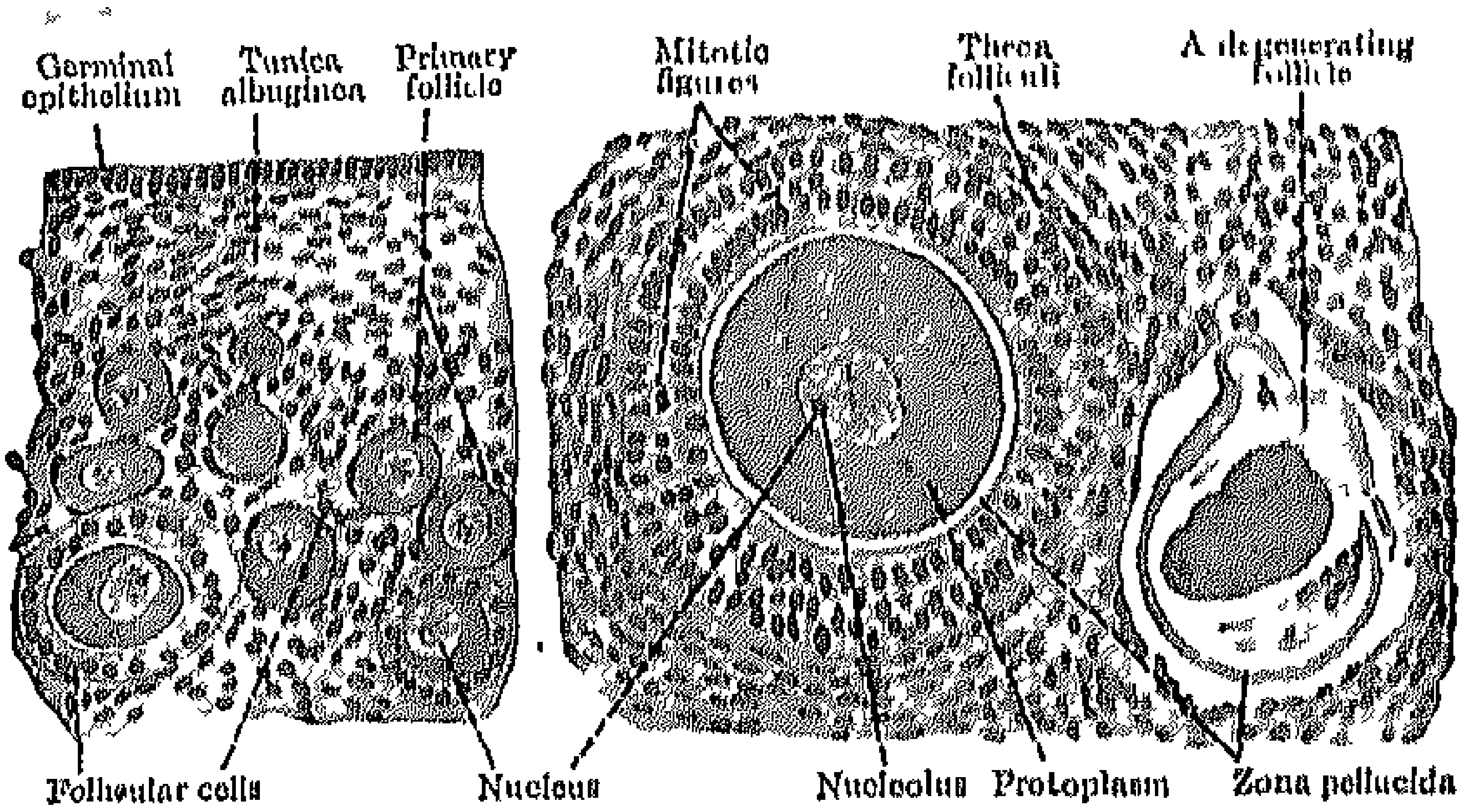


Fig. 241. From a section of a rabbit's ovary. 240 ×. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

The cortex, which surrounds the medulla except at the hilum, consists of a connective tissue stroma whose fibers are more or less loosely interwoven in all directions and contain numerous spindle-shaped connective tissue cells. Scattered throughout this cortical stroma are the *ovarian follicles*. Enclosing the cortex and separating it from the germinal epithelium is a thin layer of densely compacted fibrous tissue known as the *tunica albuginea*. The fibers of this layer are more regularly arranged and there are fewer cells than in the adjacent portion of the cortex. External to the tunica albuginea are the cells of the germinal epithelium which rest directly on this dense fibrous layer (apparently there is no intervening basement membrane). In the young ovary these cells are cuboidal, becoming flattened in the adult stage. The surface of the ovary is marked by a number of irregular, more or less spherical bulgings due to the presence of the characteristic structures of the ovary—the *ovarian* or *Graafian follicles*. These follicles, which are located only in the cortex, may become so distended with follicular fluid as they mature, that they have the appearance of being partly located in the medulla.

The medulla consists of a fibroelastic stroma which is continuous at the hilum with the connective tissue of the broad ligament. Its loosely interwoven tissue contains numerous blood and lymphatic vessels and nerves. In the region of the hilum, smooth muscle is scattered throughout this tissue. In some ovaries there are also vestigial fetal structures in this area. These structures usually appear as tubules or strands of epithelial cells, and represent remnants of the embryonal mesonephros.

The follicles are the structures which are associated with the development of the ovum. They vary in number depending on the age of the individual, being more numerous in newborn infants than in later years. The estimates that have been made vary so widely that no definite statement can be given as to the number present at any given period. It is probable that the total number (in both ovaries) at the time of birth, exceeds 100,000. This number diminishes as age advances, so that at the close of the childbearing period or shortly thereafter, the follicles have almost disappeared. During the time between sexual maturation and menopause, it has been estimated that about 400 mature ova are produced, the rest of them degenerate and never reach maturity.

According to the stage of development in which they appear, the follicles are sometimes designated as *primary*, *intermediate*, and *mature*.

The primary follicles arise from the cells of the germinal epithelium during the period of embryonic development and occur most abundantly in the ovaries of the young. They are located in the part of the cortex which lies immediately beneath the tunica albuginea. In fact they are so numerous in this region that it might almost be considered as a separate layer. The diameter of a primary follicle varies

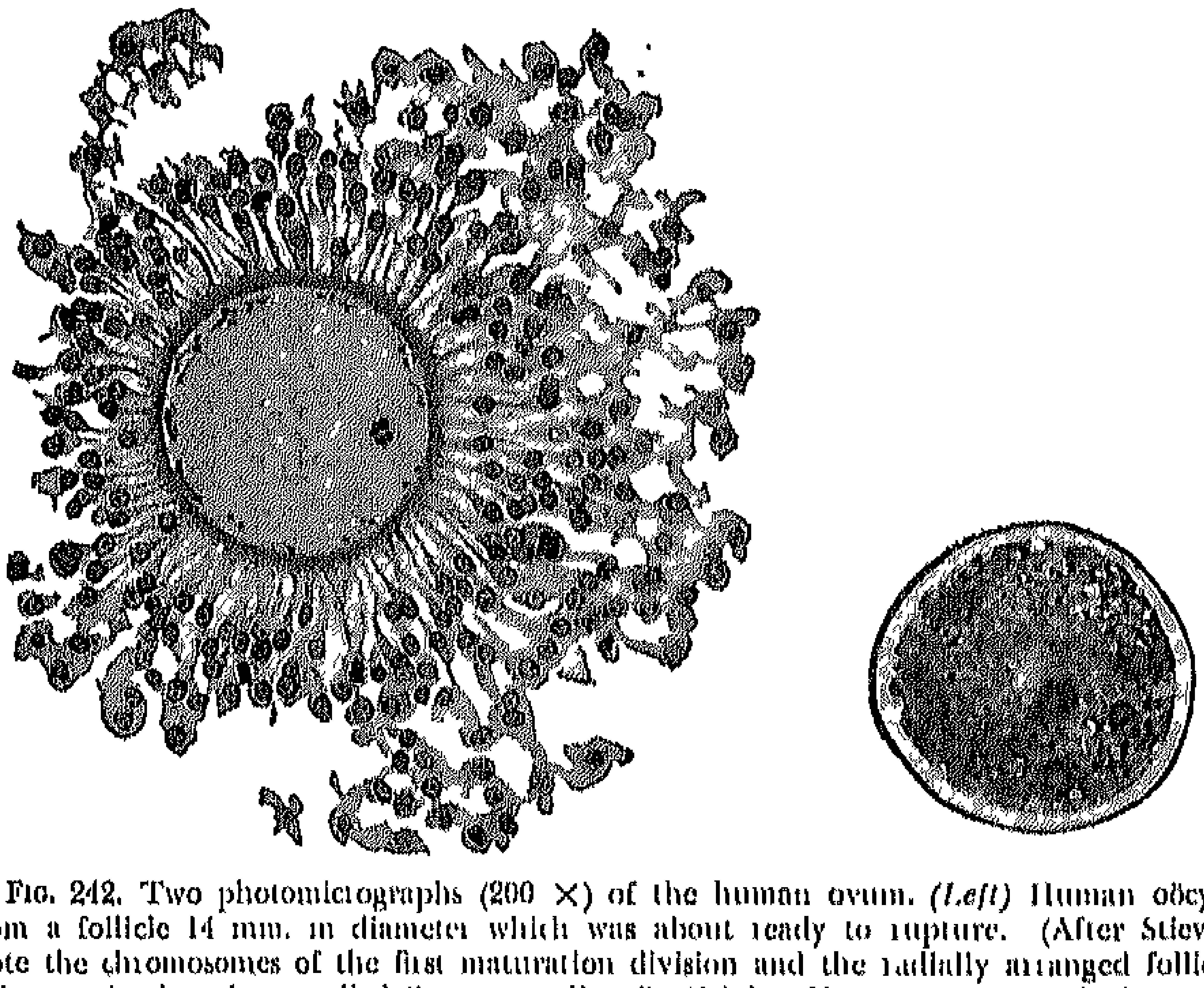


FIG. 242. Two photomicrographs (200 ×) of the human ovum. *(Left)* Human oöcyte from a follicle 14 mm. in diameter which was about ready to rupture. (After Stieve.) Note the chromosomes of the first maturation division and the radially arranged follicle cells constituting the so-called "corona radiata." *(Right)* Human ovum washed out of the uterine tube. Photographed before fixation. (Carnegie Coll., 6289, courtesy W. H. Lewis.) Note the thickened zona pellucida and the loss of the cells which constituted the corona radiata. The small, highly refractive areas in the cytoplasm are due to lipoid droplets. (Courtesy, Patten: "Human Embryology," Philadelphia, The Blakiston Company.)

between 40 and 50 microns, each follicle consisting of an ovum enclosed by a capsular arrangement of flattened, follicular cells. The ovum is a large cell, having a pale staining granular cytoplasm and a vesicular nucleus which is slightly eccentric in position. The nucleus is enclosed by a sharply defined nuclear membrane, and contains a wide-meshed network of linin fibers and a scanty amount of granular chromatin. A deeply stained, spherical nucleolus is also present. Externally the follicle is surrounded by the connective tissue of the cortex. In the primary follicles the nucleus may be enveloped by a light area of granular cytoplasm which is called the *vitelline body* or *yolk nucleus of Balbiani*.

A relatively small number of the follicles reach maturity. If they do, the process by which the mature condition is attained, may be indicated as follows:

Stage 1. The ovum increases in size. Yolk granules appear as highly refractive, spherical bodies in the cytoplasm. A distinct cell membrane is developed about the surface of the ovum, which gradually increases in thickness and forms the *zona pellucida*. The follicular cells become first cuboidal and then columnar, and multiplying by mitosis, surround the ovum with several cell layers. As the process of growth continues, the follicle shifts its position from the periphery to the deeper part of the cortex. The object of this shift is to secure a more favorable location in the stroma for its continued expansion.

Stage 2. As the follicle continues to increase in size, small spaces appear between the cells. These spaces are formed by an accumulation of a clear, watery fluid which presses the cells apart. With the continued growth, these spaces enlarge and finally unite to form a single cavity which is filled with the follicular fluid. From this point the growth of the follicle to the mature condition progresses rapidly.

Stage 3. In this stage the mature condition of the follicle has been attained. Its wall consists of several layers of cells, the *stratum granulosum*, which encloses a large cavity, the *antrum*. The antrum is filled with a clear, watery fluid, the *liquor folliculi*, in which there is a considerable amount of protein. When precipitated by the reagents employed in the preparation of the tissue, the follicular fluid has a granular appearance.

The ovum does not come into contact with the fluid in the antrum, but is embedded in a moundlike accumulation of follicular cells, the *cumulus oöphorus*, or *discus proligerus*. The cells of the cumulus, which immediately surround the ovum, as well as those at the periphery of the follicle, are columnar, while the cells which border the antrum are more or less stellate in form and are said to have anastomosing processes. The remaining cells of the stratum granulosum are polyhedral in form.

The connective tissue immediately surrounding the follicle is organized to form a capsular investment, the *theca folliculi*. This consists of an outer fibrous and an inner vascular layer. The outer layer is formed by closely interwoven collagenous fibers and their fibroblasts and is known as the *theca externa*. The fibers of the vascular layer are more loosely arranged and support numerous blood vessels. This layer is known as the *theca interna*. The connective tissue cells of the theca interna increase in size and accumulate in groups near the surface of the stratum granulosum. No clearly defined line of division exists between the fibrous and vascular layers of the theca.

The fully matured Graafian follicle is a large vesicular structure occupying the entire depth of the cortex, a portion of which is frequently pressed into the medulla. Due to a continued increase in the amount of the follicular fluid, the intrafollicular pressure causes the vesicle to expand and form a rounded bulge on the surface of the ovary. The tall, columnar cells surrounding the ovum are radially arranged and are known as the *corona radiata*. In the Graafian follicle, the ovum has come to be a large cell with a diameter of 100 microns or more. Its cytoplasm is filled with highly refractive, spherical granules of a substance known as *deuteroplasm (yolk)*. Its large, vesicular nucleus is eccentric in position and is enclosed by a sharply defined nuclear membrane. It contains a network of linin fibers and a few, scattered granules of chromatin. The nucleolus is large, spherical and stains deeply.

The cytoplasm of the ovum is enclosed by a thick membrane, the *zona pellucida*. It seems very likely that the zona pellucida is the product of the follicular cells. It has a striated appearance, due to the presence of minute channels through which delicate protoplasmic processes from the cells of the corona radiata extend for the purpose of conveying nutritive material to the ovum. Yolk granules are absent from a narrow area immediately beneath the zona pellucida. This area is known as the *perivitelline space*.

The discharge of the ovum from the Graafian follicle is known as *ovulation*. The mature follicle moves toward the surface of the ovary, clefts appear between the cells of the cumulus which becomes loosened from the stratum granulosum. Surrounded by a few cells of the cumulus, the ovum floats more or less freely in the liquor folliculi. The pressure of the constantly increasing amount of fluid causes the wall of the follicle to expand and become quite thin, especially in the area that bulges above the surface of the ovary where it is not supported by a surrounding stroma. An area in the bulging wall, known as the *stigma*, becomes particularly attenuated and avascular. Rupture occurs at the stigma and the follicular fluid, together with the ovum in its corona radiata, oozes from the opened wall. The process is gradual, not cataclysmic as has been claimed by some writers.

Various explanations have been presented to account for the rupture of the follicle and the discharge of the ovum, but none of those which have been offered is completely acceptable.

Ovulation in humans occurs normally at regular periods of about 28 days. The rupture of the follicle usually does not coincide with the menstrual periods, but takes place during the intermenstrual phase. Ordinarily a single ovum is discharged at each ovulation, although two or even more may be liberated at one time. The evidence favors the belief that the ovaries alternate in the maturation and discharge of an ovum.

The conditions which insure the passage of the ovum into the fimbriated end of the Fallopian tube (uterine tube or oviduct) are obscure. Observations which have been made on some of the lower animals indicate that the *fimbria* are clasped about the surface of the ovary during this time and that the ovum is carried into the duct by currents formed through the action of the cilia which are borne on the free surface of the cells lining the fimbria. Passage of the ovum along the tube is effected primarily by contractions of the tubal musculature, the cilia playing probably no more than a minimal role. Experiments have been performed which show that if one ovary is removed and the tube on the opposite side is tied or removed, the ovum expelled from the remaining ovary may cross the pelvis and gain access to the uterus by way of the opposite, patent uterine tube. However, no active migration of the ovum may be involved since observations during operations on women indicate that the fimbria of one tube may be applied to the opposite ovary.

Of the primary follicles contained in the ovary at birth, only a relatively small number reach maturity. The majority degenerate and disappear. The progressive change which ends in the destruction and removal of the follicles is called *atresia*. The period in which these degenerative changes are most active, is between the time of birth and the age of puberty. After puberty atretic changes take place at a somewhat slower rate. In follicles which are undergoing atresia, the ova shrink and break into fragments. This cellular debris is ingested by the follicular cells, which in turn degenerate and are finally destroyed. In the cortex, the place which was occupied by the follicle becomes filled with fibers from the surrounding stroma.

In the follicles in which the growth process has begun, the changes follow a similar course up to the replacement of the degenerative ova by connective tissue from the stroma. In these follicles, however, the zona pellucida may remain as a folded glassy membrane after the other elements have disappeared.

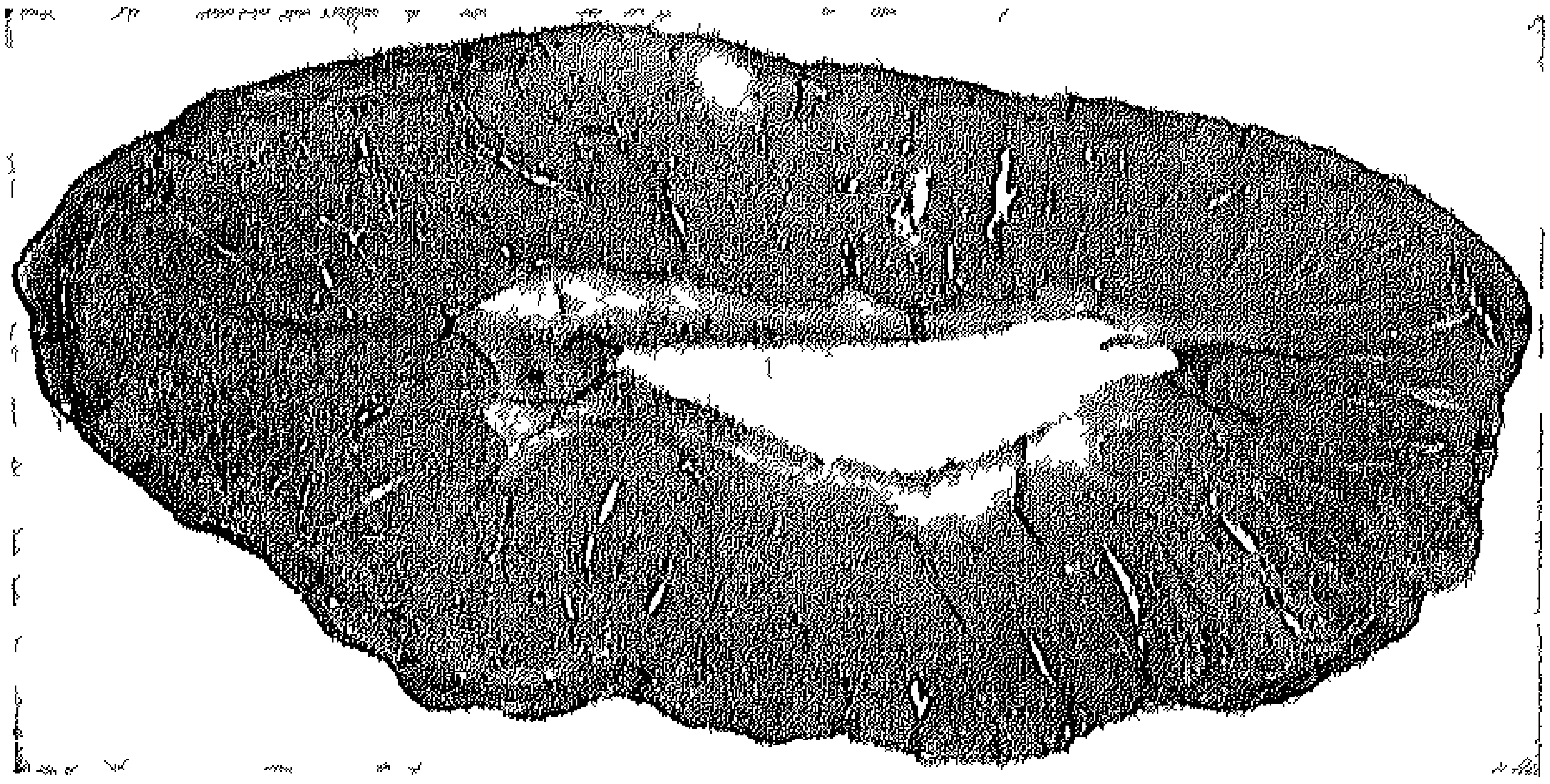


FIG. 243. Section through a corpus luteum from a human ovary. Photomicrograph.

The process which leads to atresia of follicles that are approaching maturity is somewhat more complicated. The cells of the stratum granulosum become softened and float off into the follicular fluid. Those which line the antrum are the first to be affected, while those surrounding the ovum resist the change for a much longer time. The connective tissue from the theca interna pushes its way into the follicle. The theca itself becomes folded, and its cells, which develop a yellow color due to an accumulation of lutein pigment, resemble a corpus luteum *(corpus luteum atretica).* After the degeneration of the ovum, the zona pellucida persists in a collapsed condition and may be identified in the mass of degenerated follicular tissue. The fibroblasts of the theca interna are transformed into large, polyhedral cells which are broken up into groups by the invasion of bands of fibrous tissue. These groups of thecal cells may persist for some time in the tissue of the cortex where they are known as interstitial cells. Interstitial cells are more numerous in the cortex of the ovary during the earlier years of life. They soon degenerate and disappear, however, and are rarely found during the later years.

It appears to be fairly well established that the interstitial cells do not form a secreting body in the tissue of the human ovary, as was once supposed to be the case. These cells are from the theca interna of the atretic follicles, which accounts for their abundance during the earlier years of life, when follicular atresia is most actively taking place.

MATURATION OF THE OVUM

The ovum is formed by a succession of divisions by which the chromatic material of its nucleus is reduced to an amount representing one-half of the normal or somatic number of chromosomes. The process by which this reduction is accomplished is called *maturation*.

The cells from which the ova are derived, and which correspond to the spermatogonia, are called *oogonia*. Several generations of these cells are produced during the period of embryonic development. At birth the majority of the oögonia have passed through a period of growth, their chromosomes uniting by *synapsis* to form one-half the somatic *(haploid)* number. The cells in which this has taken place correspond to the primary spermatocytes, and are known as *primary oocytes*. The *secondary oöcytes*, which correspond to the secondary spermatocytes, are derived from the primary oöcytes by division. Each chromosome splits longitudinally and transversely, forming a tetrad. A small globule of protoplasm protrudes from the side of the oöcyte. It receives a dyad from each tetrad and is pinched off, forming the *first polar body*. This is followed by the reorganization of the spindle, and the extrusion, from the body of the cell, of another globule of protoplasm which receives a monad from each remaining dyad, and is split off from the parent cell to form the *second polar body*. The cell, which corresponds to a spermatid, is now a fully matured ovum and is prepared by this reduction of its chromatic material for union with the sperm *(fertilization)*. Although the time relations for these maturation divisions in the human being are uncertain, it is believed that they are similar to those in most other mammals. As a rule the first polar body is produced shortly before ovulation, and the remaining chromosomes proceed immediately to form a spindle figure. However, the second division is not completed until after ovulation and fertilization have occurred.

Ovulation is followed by certain changes which take place in the follicle. After liberation of the ovum, the wall of the follicle collapses and is arranged in a series of folds. The theca externa remains unchanged. The fibroblasts of the theca interna increase in number, become hypertrophied and collect in masses in the angles between the folds of the stratum granulosum. A small amount of blood from the capillaries which have been ruptured by the passage of the ovum flows into the cavity of the follicle and mingles with the fluid that remains.

Following the discharge of the ovum and the collapse of the follicular wall, the cells of the stratum granulosum enlarge and there is an increase in the number of cell layers. The cytoplasm of the cells acquires a lipoidal substance, called *lutein*. Cells containing this lutein substance are called *lutein cells*, and the follicular space which is now partly filled with these cells is known as the *lutein body* or *corpus luteum*. The human corpus luteum rarely, if ever, becomes a solid body as is true in some other mammals.

Strands of connective tissue and small blood vessels penetrate between the lutein cells and form a highly vascular layer that covers the inner surface of the ruptured follicle. The cells from the theca interna, which have accumulated in masses between the folds of the corpus luteum, also develop lutein in their cytoplasm (*thecal lutein cells*), and differ from the lutein cells of the granulosa (*granulosa lutein cells*) only in being somewhat smaller. The human corpus luteum reaches its highest development about 12 days after ovulation and has a slightly yellow color due to the lutein in the cells. It is called a *corpus luteum of menstruation* or *corpus luteum spurium* and through the production of progesterone and estrogen plays an important role in the post-ovulatory phase of the menstrual cycle.

If the discharged ovum escapes fertilization, menstruation follows in about 14 days after ovulation as a result of failing function of the corpus luteum. Degeneration of the corpus luteum, apparently due to the lack of continued stimulation by gonadotrophic hormone, can be first detected in the lutein cells where the lipoidal droplets are enlarged and coalesced. The cells decrease in size and connective tissue increases. In some instances blood is extravasated from the capillaries and may accumulate in the central cavity together with a loose gelatinous connective tissue. Hyalinization follows slowly and the size of the corpus luteum decreases progressively. After a period of several weeks the entire structure is a whitish scar, the *corpus albicans*, which will persist for many months. Its function ceases before the onset of menstruation.

If the ovum is fertilized, conditions arise which cause the corpus luteum to become more persistent. These conditions are not known with any degree of certainty, but it is supposed that the production of gonadotrophin by the implanted ovum is responsible for the maintenance of the corpus luteum. It is then known as the *true corpus luteum (corpus luteum verum)*. The corpus verum is appreciably larger than the corpus spurium and its constituent cells are both larger and more numerous. Production of progesterone and estrogen increase during this time. Early in the third month of pregnancy the corpus verum undergoes degenerative changes. These proceed throughout the remainder of pregnancy and while the corpus is present at the time of childbirth its hormonal activity has ceased some time earlier. Indeed, the human corpus luteum may be removed relatively early in pregnancy without interfering with the maintenance of pregnancy. This is possible since the placenta assumes the role of producing progesterone and estrogen.

THE OVIDUCTS

On being discharged from the ovary, the ovum passes to the uterus through the *oviduct* or *uterine tube*. This is a tubular structure five

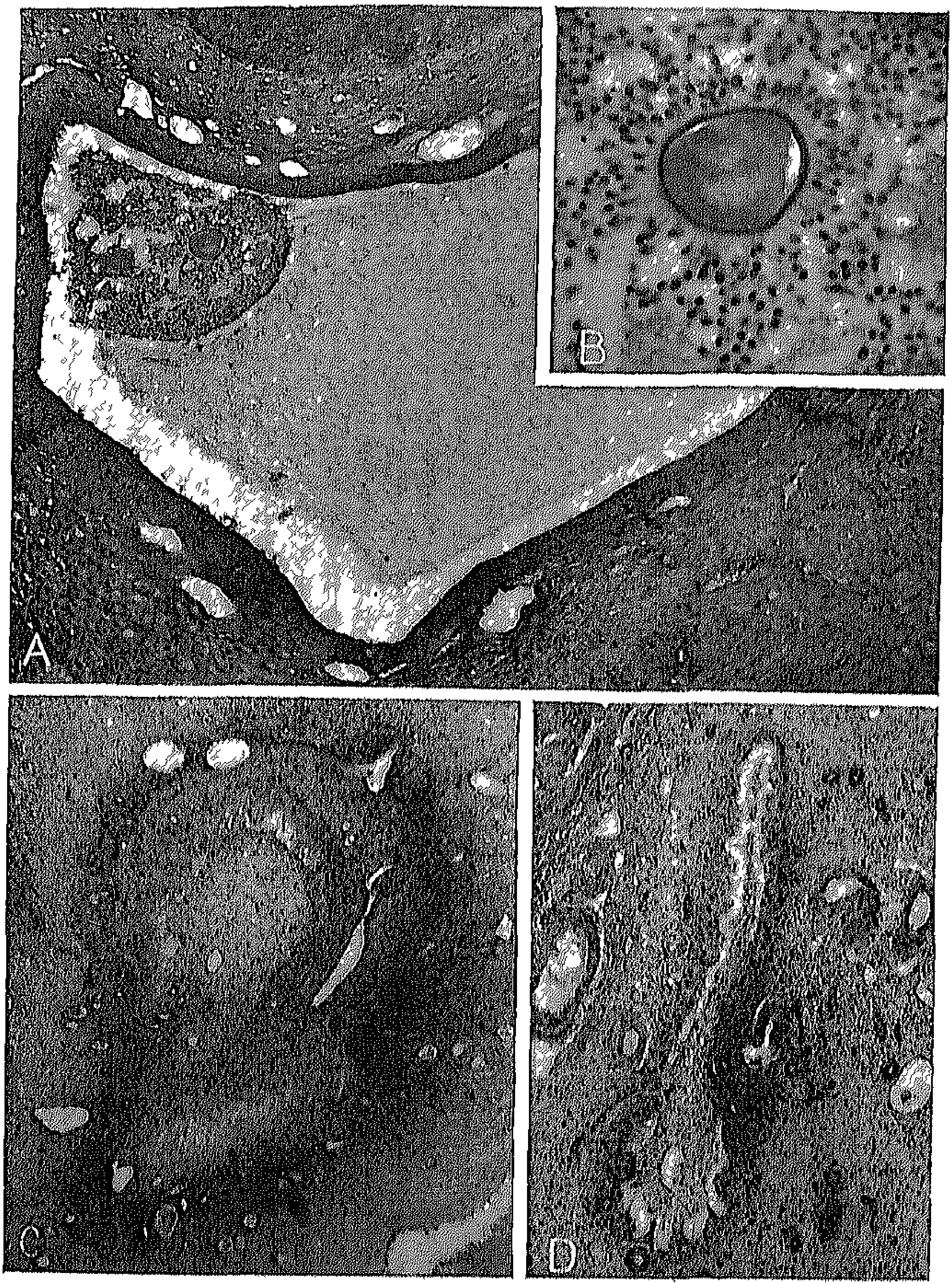


FIG. 244. Photomicrographs showing three stages in follicular atresia. (A) Early regressive changes in follicle (75 ×). (B) Ovum and cumulus cells (200 ×). (C) Antrum shrunken and filled with young fibroblasts (50 ×). (D) Scar similar to corpus albicans following a corpus luteum, but smaller (50 ×). (Courtesy, Patten: "Human Embryology," Philadelphia, The Blakiston Company.)

or more inches in length, located in the border of the broad ligament. It consists of three parts: the *isthmus*, which begins at the uterus and includes almost one-third of the total length of the oviduct; the *ampulla*, an expanded portion, nearly twice the length of the isthmus; and the *fimbriated extremity* or *infundibulum*, the distal portion of the tube which lies in close proximity to the ovary. The diameter of the oviduct is smallest in the isthmus, being slightly more than 3 mm. It increases toward the ampulla, in which it may be 7 mm. or more.

The wall of the oviduct includes three layers: a *mucosa*, a *muscularis*, and a *serosa*. The mucosa consists of a simple columnar epithelium resting on a thin stroma of delicate connective tissue fibers. Scattered through the epithelium, near the basement membrane, are small cells with relatively little cytoplasm and deeply staining nuclei. The epithelial cells are low in the isthmus, but increase in height until they appear as tall columnar elements in the ampulla. Some of the cells are provided with cilia, while others are nonciliated. The nonciliated cells are densely granular and produce a substance which is believed to provide nourishment for the ovum as it passes through the tube. The movement of the cilia is in the direction of the uterus.

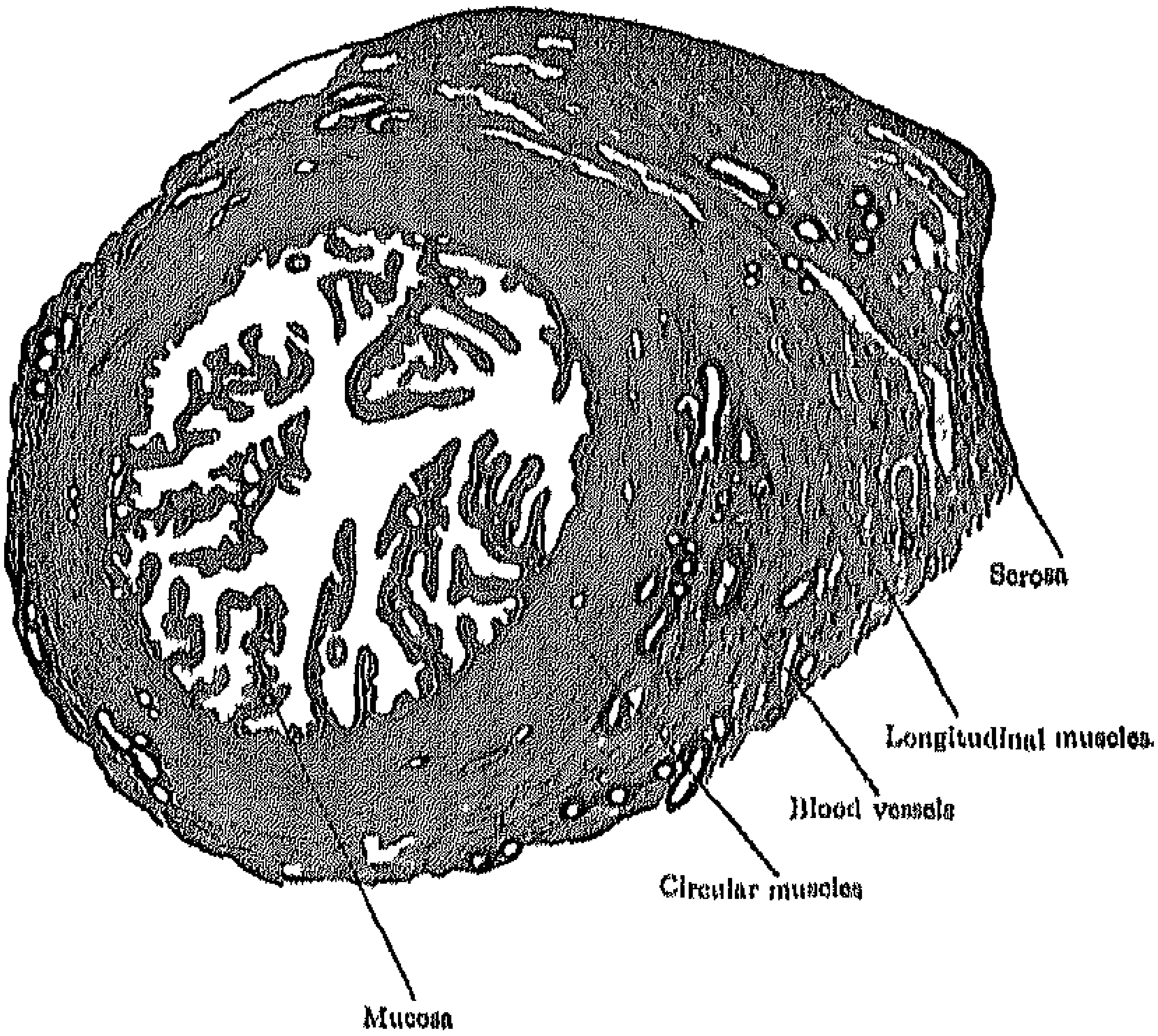


FIG. 245. Cross section, near the ampulla, of a uterine tube from an adult woman. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

The epithelium has been observed to undergo certain changes during the menstrual period. At the beginning of menstruation the cells are low; at its close they begin to increase in height; and at the mid-interval they may have acquired the appearance of being pseudostratified.

The *mucosa* is raised into a series of folds which, in the isthmus, appear as three or four broad, low ridges. Toward the ampulla the ridges become taller and narrower, and develop secondary and tertiary folds. These folds anastomose and enclose pockets which form a labyrinthine pattern. The folds are arranged about the distal end of the tube in such a way as to give it the appearance of being surrounded by a series of fingerlike fringes *(fimbriated extremity).*

The *muscularis* is thick in the isthmus and diminishes as it reaches the fimbriated extremity. It lies directly in contact with the stroma. It consists of a thick, inner layer of circularly directed smooth muscle fibers and a thin, outer layer of longitudinal fibers. The layers are broken up into bundles by septa of connective tissue which extend between them. The circular layer is most strongly developed in the isthmus, while the longitudinal fibers form a thin layer. Extending up the tube toward the fimbriated end, there is a gradual decrease in the muscular layer with the result that in the ampulla the longitudinal fibers form only a thin and incomplete layer about the tube and it disappears entirely in the fimbriated extremity of the tube.

The *serosa*, or outer covering of the oviduct, consists of loosely arranged connective tissue which is continuous with the connective tissue of the broad ligament, and forms a layer of considerable thickness between the muscularis and the layer of mesothelial cells which lie on the surface of the broad ligament. A few tubules of the *epoophoron* may be seen in sections of the oviduct which have been taken from the region of the ovary.

The blood supply of the oviduct is by branches of the uterine and ovarian arteries; their final subdivisions penetrating the subepithelial layer of the mucosa in which they may be seen as small longitudinal vessels. The blood vessels are accompanied by lymphatics, of which there is a rich supply.

The nerves are distributed to the muscle bundles and the mucosa.

The passage of the ovum into the fimbriated extremity of the oviduct is probably brought about by certain vascular changes which take place during ovulation. The vessels in the fimbria are charged with blood causing these processes to become turgid, a condition which holds them close to the surface of the ovary. The ovum is swept into the opening of the tube by the currents set up by the action of the cilia.

The passage of the ovum to the uterus is probably due to the peristaltic contractions of the muscular wall of the oviduct. This action

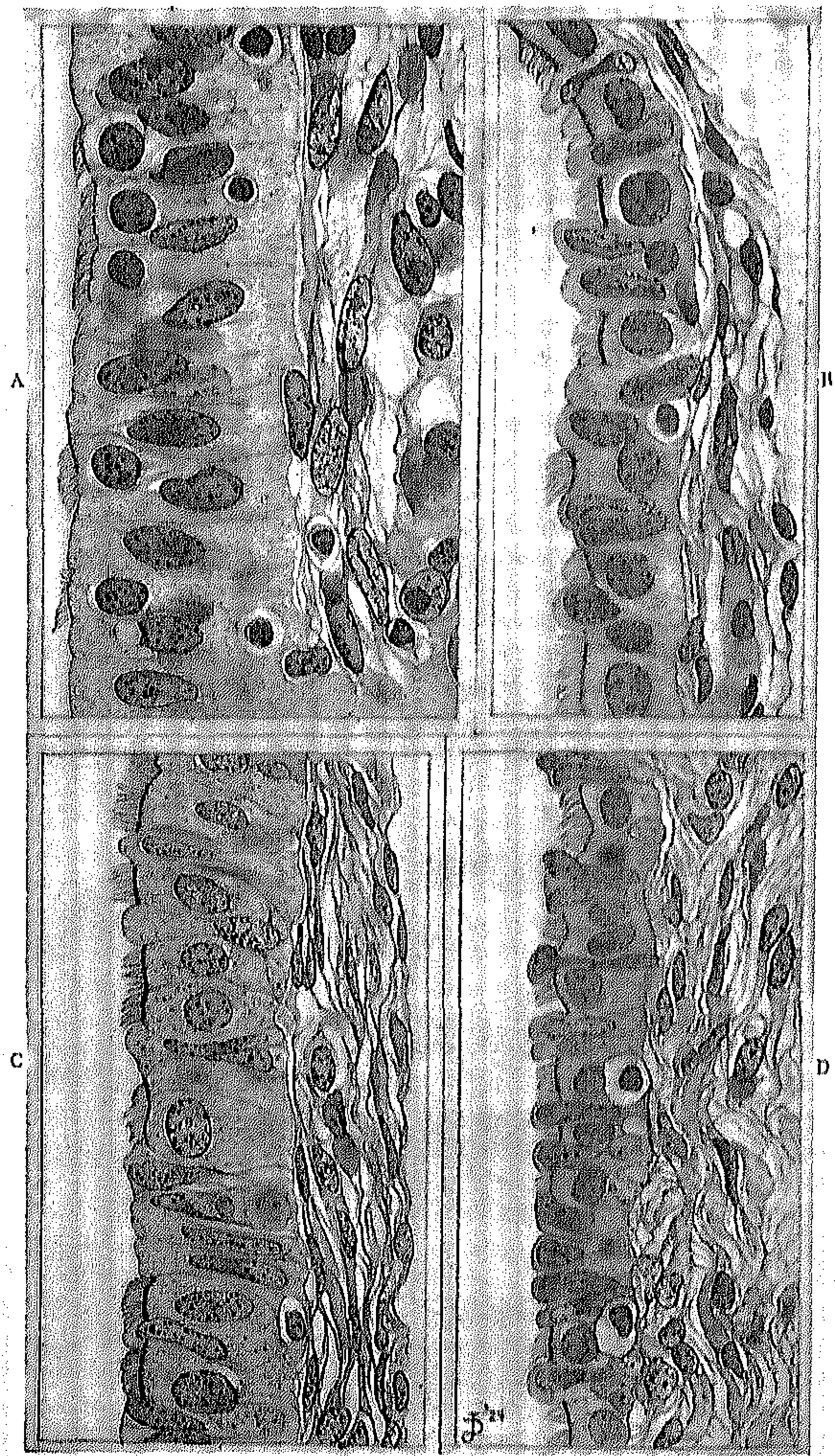


FIG. 246. Epithelium of human Fallopian tube showing physiological changes. 700 ×. (After Snyder, 1924.) (A) Mid-interval. (B) Pre-menstrual. (C) Late interval. (D) Pregnancy. (Courtesy, Cowdry: "Special Cytology," New York, Paul B. Hoeber, Inc.)

probably is not aided materially by the cilia which, in all probability, stimulate the passage of the spermatozoa by positive thigmotaxis, to move toward the distal end of the oviduct where the fertilization of the ovum usually takes place.

Extrauterine pregnancies occur in the oviduct and, more rarely, in the abdominal cavity. Although a false placentation may result from the lodgment of the ovum in these localities, development is never completed. The tissue degenerates and is removed by absorption, or, as is frequently the case, the condition is relieved by surgical procedure.

THE UTERUS

The uterus is a thick-walled, pear-shaped, muscular organ located in the pelvic cavity between the bladder anteriorly and the rectum posteriorly. Although some variation occurs in normal nulliparous women, the uterus averages about two and one-half inches in length, one and three-fourths inches in breadth, and about one inch in thickness. It is flattened in the antero-posterior direction. In women who have borne children it is somewhat larger.

The organ consists of a *body*, an expanded upper portion, the *fundus*, and a constricted lower portion, the *cervix*, which opens into the vagina. The cavity of the uterus is triangular in outline, the oviducts opening into its upper laterally expanded fundic portion. The cavity narrows in the body and as the *cervical canal* passes through the cervix to open into the vagina. The point where the uterine cavity enters the cervical canal is known as the *internal os*, while the opening of the cervical canal into the vagina is called the *external os*. Two vertical folds, one on the anterior and one on the posterior wall of the cervical canal, are known as the *plicae palmatae*.

The wall of the uterus consists of three layers: an internal layer, the *mucosa (endometrium)*; a middle layer, the *muscularis (myometrium)*; and an external layer, the *serosa (perimetrium)*. The *mucosa* consists of a simple columnar epithelium, the cells of which are taller in the cervix than in the body and fundus, glands and a fibrocellular stroma. The glands extend throughout the entire endometrial layer. During menstruation the outer portion of the endometrial layer, called the *functional layer*, is more or less completely sloughed off. The part of the endometrium which contains the basal portion of the glands *(basal layer)* is retained. It is the basal layer which contributes to the regeneration of the endometrial layer during the proliferative phase of the menstrual cycle. Some of the surface cells of the endometrial layer are provided with cilia, although the epithelium as a whole is not consistently ciliated. Where present, the cilia beat in the direction of the cervix. The lower end of the cervix is lined by a stratified squamous epithelium which extends into it from the vagina. After childbearing, the stratified epithelium may extend into the cervical canal for one-half or two thirds of its length.

The stroma on which the epithelium rests reveals its embryonic character by the delicate reticular fibers of which it is composed, and by the number and character of the connective tissue cells it contains. In their irregular form, large nuclei and branched processes, they resemble the cells of embryonic mesenchyme. In addition to the connective tissue cells, lymphocytes, granular leucocytes and macrophages may be present in the tissue spaces. The tissue of the stroma is continuous with that of the oviducts and it is also continuous, through the cervix, with the subepithelial tissue of the vagina. As it is continued into the cervix, the stroma loses its embryonic character and the fibers become coarser and take on the appearance of mature connective tissue.

The epithelium in the body of the uterus is invaginated to form the simple, tubular uterine glands. Some of these glands show bifid terminal portions. These glands follow a winding course and extend deeply into the stroma, their blind ends being located, in some instances, among the muscle bundles of the adjacent portion of the muscularis. The epithelium of the glands is similar to that which forms the lining of the uterus. Some of the cells bear cilia, the movement of which is toward the surface of the mucosa.

Only the distal portions of the uterine glands undergo cyclic changes in structure, the basal portions serving to restore the epithelium of the surface of the mucosa after it has been destroyed by the changes which take place during menstruation. The cells which form the lining of the gland are pushed upward and onto the surface, as new cells are formed beneath them. The replacement of the epithelium of the mucosa by the proliferation of the cells of the glandular epithelium is indicated by the number of mitotic figures which appear in the upper portions of the glands in the postmenstrual period.

The columnar cells which form the epithelial lining of the upper part of the cervical canal are taller than those in the body and fundus of the uterus. The free surfaces of these cells are frequently provided with cilia. The tubular glands of the cervix, formed by the invagination of its epithelial lining, are extensively branched. These glands produce a clear, mucoid secretion that is thought to contribute to the formation of the vaginal plug. In some of the glands this mucous secretion may be retained in their deeper portions, causing them to become distended and cystlike. These cystlike dilatations of the cervical glands are known as the *follicles* or *ovules of Naboth*.

The *muscularis* forms the thickest portion of the wall of the uterus. It is composed of smooth muscle intermingled with septa of connective tissue. The muscle fibers are of unusual length and branch in a manner suggestive of cardiac muscle. The muscle bundles are arranged in poorly defined layers, which may be designated as an inner layer of longitudinal fibers, a middle layer of circular fibers, and an outer layer of longitudinal fibers.

The irregular manner in which the fibers intermingle, makes it difficult to ascribe them to definite layers. An attempt has been made to define the fiber zones of the uterine muscularis by the general, rather than by the particular, direction which the fibers follow: (1) The *stratum submucosum*, a thin layer immediately external to the mucosa, in which the fibers are mainly longitudinal in direction with an intermingling of obliquely, or circularly, directed bundles. (2) The *stratum vasculare*, the most strongly developed portion of the muscularis, the fibers being mostly circular in direction. Between the fiber bundles are numerous, thin-walled venous spaces, from which the layer receives its name. (3) The *stratum supravasculare*, in which the muscle fibers are mainly longitudinal, but with an interweaving of fibers that are oblique, or circular, in direction. (4) The *stratum subsera*, the part of the muscularis which lies internal to the serosa, the fibers of which are longitudinally directed. The stratum submucosum and stratum supravasculare are regarded by some anatomists as subdivisions of the circular layer.

The *serosa* is a layer of fibroelastic tissue which lies external to the muscularis. This tissue supports a layer of mesothelial cells, on the anterior and posterior walls of the uterus, which is continuous with the peritoneal lining of the abdominal cavity. On the lateral borders of the uterus the connective tissue is continuous with that of the broad ligament, and is known as the parametrium. The twisted uterine arteries are located in the parametrium, their convolutions enabling them to adjust to the expansion of the gravid uterus.

The wall of the cervix has a firm consistency due to the densely compacted fibroelastic tissue of its mucosa. The smooth muscle fibers are arranged in an inner circular and an outer longitudinal layer. Except for the absence of the inner longitudinal layer the arrangement of the muscular tissue in the cervix is similar to that in the body of the uterus. However, the layers are somewhat more clearly defined.

The blood supply of the uterus is by way of the uterine arteries. These vessels enter the uterus on its lateral walls and extend into the muscular layer where they branch. The branches extend toward the midline of the organ, one set of branches going around the front, the other around the back of the uterus to anastomose in the midline area with branches from the opposite side. These vessels are known as the arcuate arteries. From these arcuate arteries two sets of branches arise. One set goes toward the periphery of the organ to supply the outer layers of the muscular coat. The other set extends toward the lumen to supply the inner muscular and endometrial layers. This latter set of arteries may be subdivided according to arrangement and distribution. One group of these, the straight arteries, penetrate the endometrium and end in a "tufted" arrangement in the basal part of the endometrium, which is the area they supply. The second group starts from the arcuate artery as straight arteries and become tortuous as they pass through the inner muscular layer. They are known as the spiral or coiled arteries. They extend the entire width of the endometrium and their terminal branches form small vascular tufts to supply the functional layer of the endometrium. The veins of the uterine wall correspond in position and arrangement with the arteries.

The lymphatics are in the form of networks in the mucosa and muscularis, from which vessels join the larger lymph channels in the serosa. The lymph leaves the wall of the uterus in vessels which extend through the broad ligament and join the main lymph trunks in the pelvic and lower lumbar regions.

Unmyelinated fibers from the sympathetic system are distributed to the walls of the blood vessels and to the muscular tissue. Myelinated fibers from the third and fourth sacral nerves are believed to form a scanty plexus beneath the epithelium. The endings of these nerves have not been fully studied.

THE MENSTRUATING UTERUS

From puberty to the age of 45–50 years, the uterus undergoes a series of periodic changes. These changes, which occur in cycles of 25–33 days (average about 28 days), are correlated with changes occurring in the ovary and have been outlined in various ways. One of these is as follows:

1. PERIOD OF REPAIR. This period begins with the close of menstrual bleeding and lasts for about two days during which the surface of the uterine cavity is re-epithelized by cells migrating from the basal ends of the uterine glands.

2. PERIOD OF PROLIFERATION. Extends from the close of the period of repair to about the fourteenth day of the average cycle. In dating cycles, the first day of menstrual bleeding is regarded as day 1. The endometrium grows considerably and the glands become long, but remain relatively straight. Ovulation occurs at the end of this period. The endometrial growth which is seen in the proliferative period is under the control of estrogenic hormone. As a rule, particularly in long cycles, a period of rest occurs between the period of repair and the period of proliferation. In short (21-day) cycles this period may be absent while in long (35–40-day) cycles it may last for a week.

3. SECRETORY PERIOD. Extends from ovulation and formation of corpus luteum to the onset of menstrual bleeding, i.e., from about day 14 of the average cycle through day 28. During the major portion of this time the endometrium continues to grow, but in addition the glands enter into a secretory phase. They become elongated, tortuous and coiled and the constituent cells secrete glycogen, mucoid material,

and fat. The changes in the endometrium during the secretory phase are under the control of progesterone and estrogenic hormone.

4. PERIOD OF MENSTRUATION. The secretory phase culminates in a series of changes which terminate in death and desquamation of the functional portion of the endometrium and bleeding. This period varies in length, but in most women has a duration of four or five days. With the cessation of bleeding a new period of repair is initiated.

The periods of repair and proliferation are correlated with the growth and maturation of a Graafian follicle in the ovary. During the period of repair the uterine changes are characteristic of repair and regeneration. There is a multiplication of connective tissue cells which form a cellular network in which fibers are later laid down to form the thick layer of stroma typical of the resting uterus. The epithelial cells remaining in the basal portion of the glands show numerous mitotic figures and multiply rapidly to form new glands and to epithelize the denuded surface of the equally rapidly developing stroma. In a relatively short time (approximately two days) the endometrium is resurfaced and early growth has begun.

The period of proliferation may follow the period of repair almost immediately or there may be a lag of several days or a week in the case of long cycles. Very extensive growth of the endometrial constituents occurs. This is particularly evident in the glands which become progressively longer, but show only a slight tendency to become tortuous during this period. There is, of course, no change in the character of the basal portions of the glands since the latter undergo little or no change during the cycle. The coiled arteries which must regenerate their distal portions during each cycle keep pace with the general endometrial growth. The stroma becomes less compact near the close of the proliferative period.

During the secretory period the endometrium reaches the height of its development. The height of the endometrium increases somewhat due to further growth, but more particularly to the progressive accumulation of interstitial fluid, which causes the stroma to have a loose appearance. The most striking change during the secretory period occurs in the glands. As a result of continued growth the glands become dilated and tortuous, assuming a saw-toothed appearance. The cells hypertrophy and enter an active secretory phase. Early in the period the secretory products, particularly glycogen, accumulate beneath the nuclei, but after the nineteenth or twentieth day they lie above the nuclei and soon thereafter glycogen and mucoid material are released into the lumina of the glands. The epithelial borders at this time have a frayed appearance in contrast to the rather smooth and even condition which is seen during the period of proliferation. The terms *premen-*

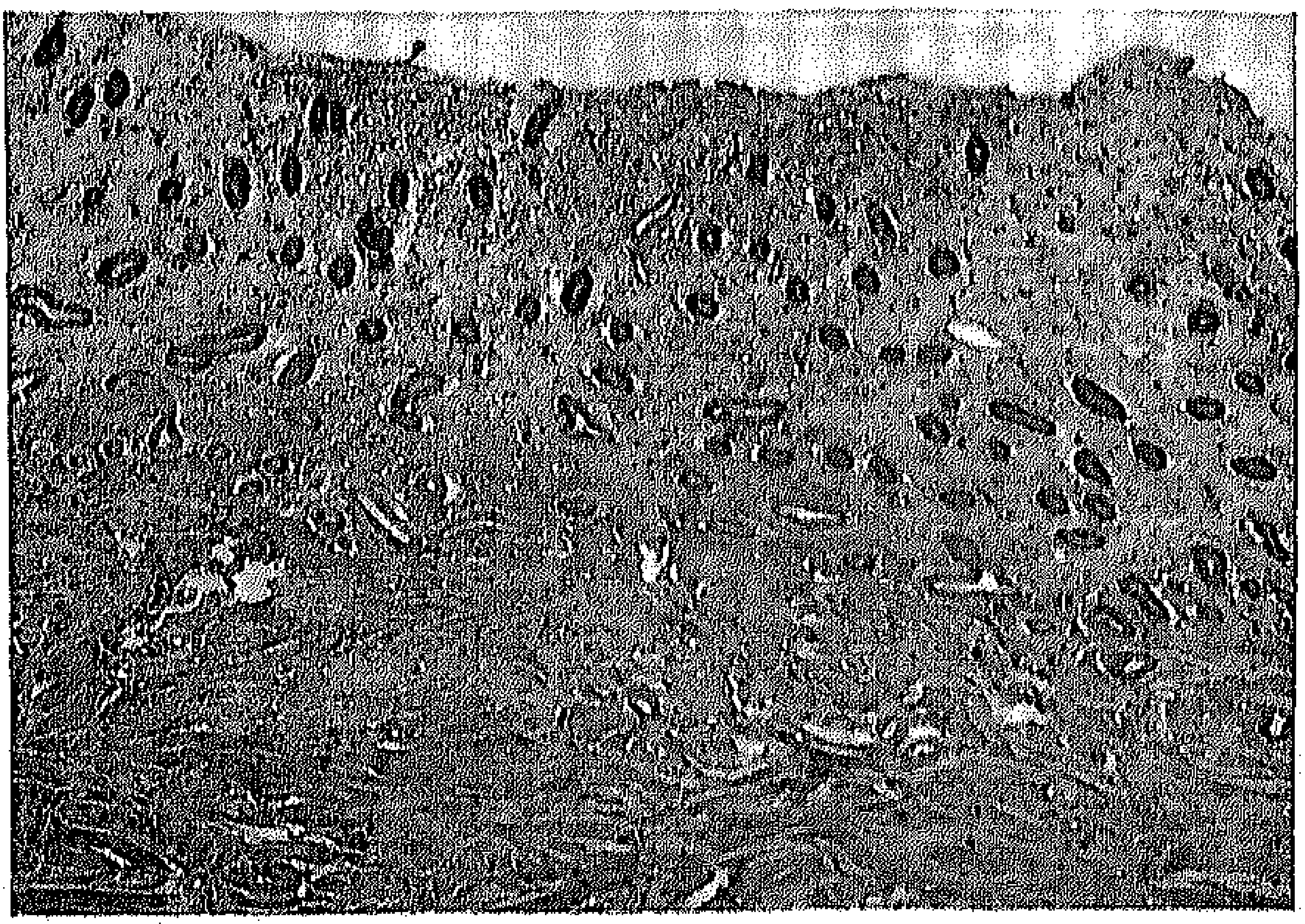


FIG. 247 A—E. (See pp. 434–436.) Sections of human endometrium taken at various stages of the menstrual cycle.

(A) Early postmenstrual stage. Tissue taken four days postmenstruum. (Courtesy, Hoffman: "Female Endocrinology," Philadelphia, W. B. Saunders Co.)

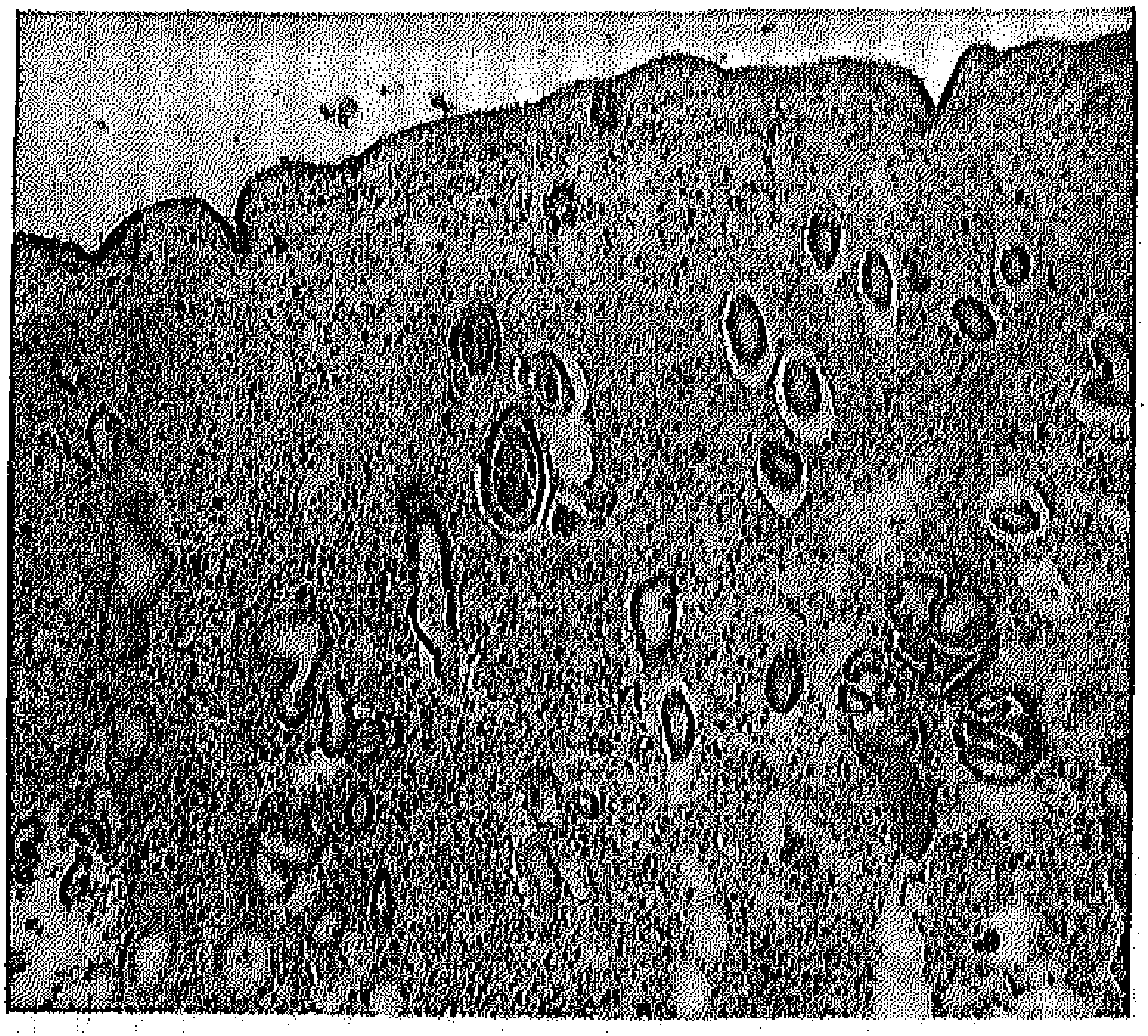


FIG. 247 (B). Proliferative stage. Tissue taken ten days postmenstruum. (Courtesy, Hoffman: "Female Endocrinology," Philadelphia, W. B. Saunders Co.)

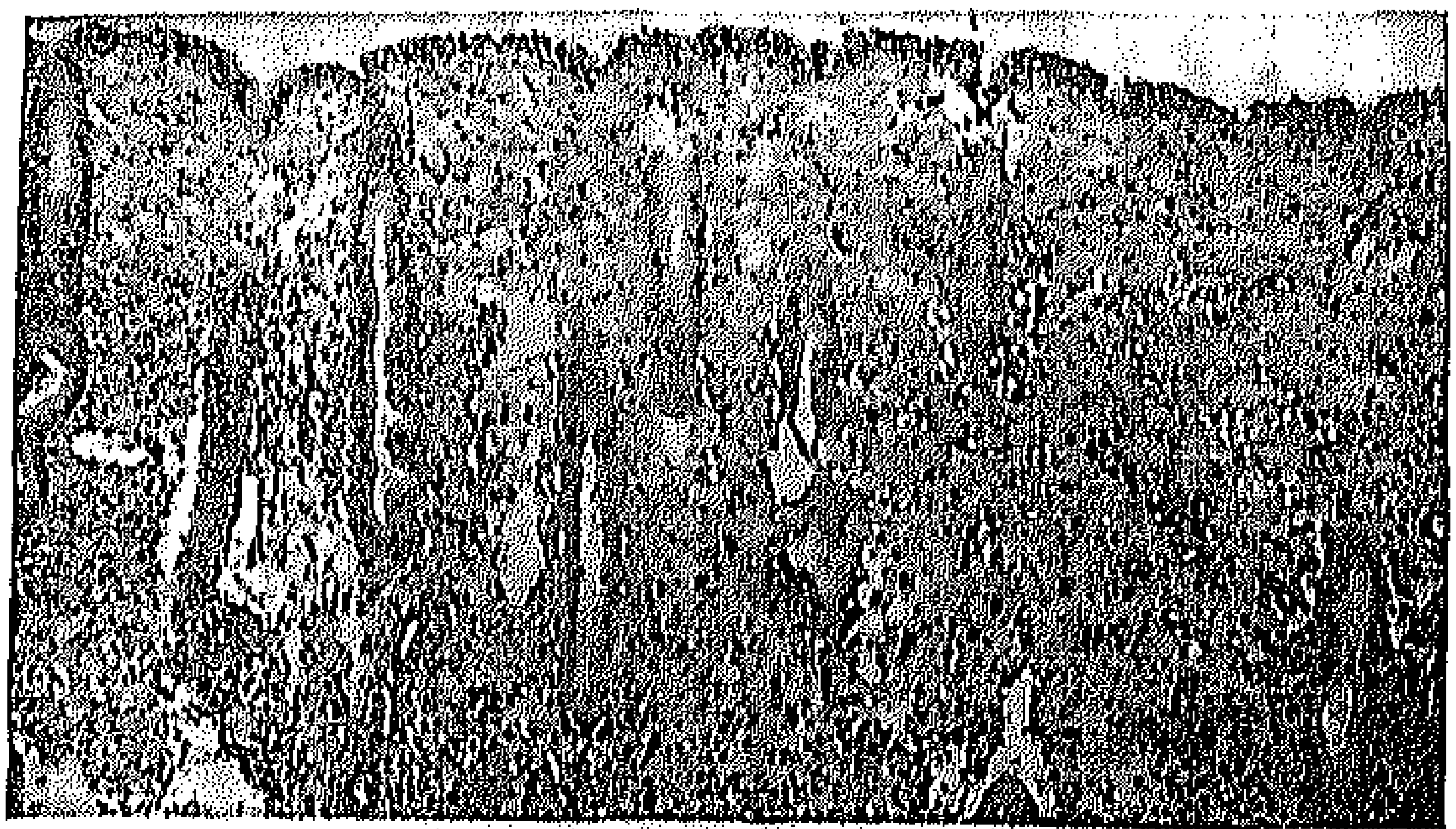


FIG. 247 (C). Early pregravid stage. Tissue taken fifteen days postmenstruum. (Courtesy, Hoffman: "Female Endocrinology," Philadelphia, W. B. Saunders Co.)

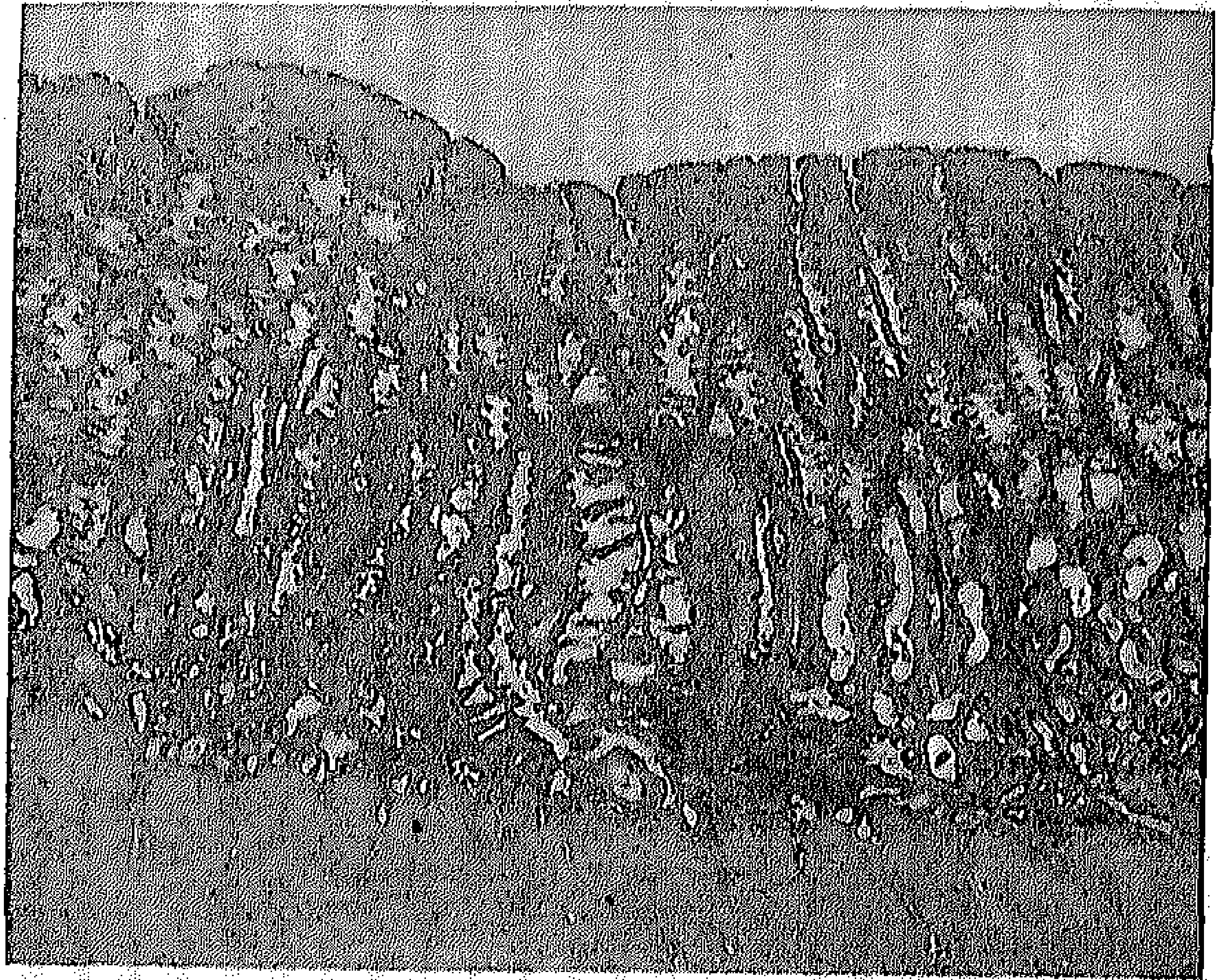


FIG. 247 (D). Pregravid stage. Tissue taken twenty-seven days postmenstruum. (Courtesy, Hoffman: "Female Endocrinology," Philadelphia, W. B. Saunders Co.)

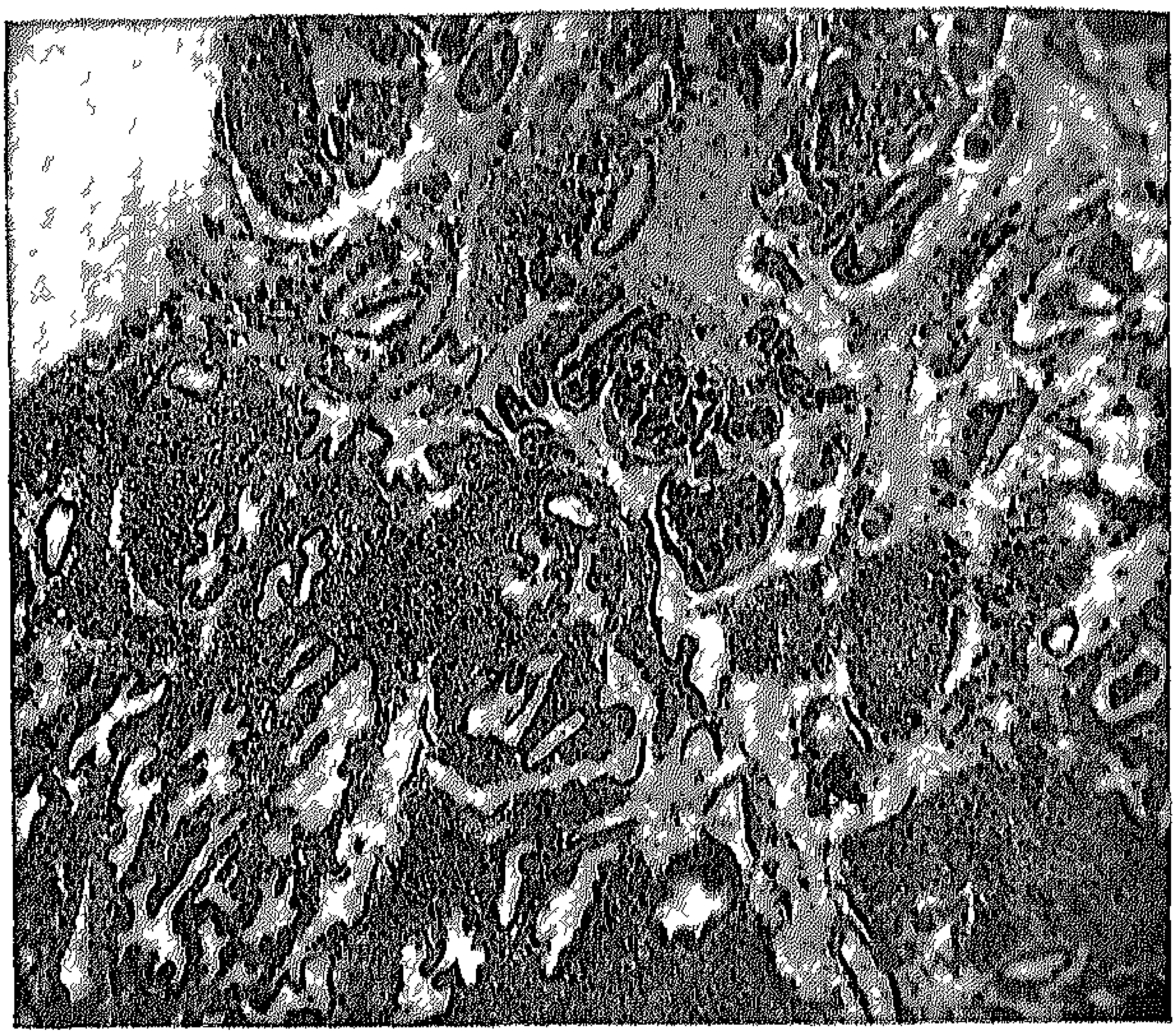


FIG. 217 (E) Menstruation. Tissue taken first day of flow. (Courtesy, Hoffman: "Female Endocrinology," Philadelphia, W. B. Saunders Co.)

strual, progravid, progestational are sometimes applied to the latter part of the secretory period since the endometrium has attained its full development and is in a state of receptivity for implantation of an ovum. The coiled arteries become progressively coiled during this period.

A day or two before the menstrual flow is visible externally, i.e., about day 26 of a 28-day cycle, the drop in levels of circulating progesterone and estrogenic hormone (due to cessation of luteal function) initiates the menstrual phase. Studies by Markee and by Phelps on endometrial bits implanted in the anterior chamber of the eye in monkeys have provided us with information which otherwise would not be available. The initial effect of lowered levels of ovarian hormone appears to be a slowing in the circulatory rate in the endometrium. This is followed by loss of interstitial fluid and shrinkage of the endometrium. The coiled arteries are compressed by the collapsed endometrium and the blood supply to the functional layer is seriously reduced. The tissues, embarrassed for oxygen, undergo necrosis and produce a vasoconstrictor substance, presumed to be similar to *necrosin*.

This substance acts on the basal portions of the coiled arteries (where they traverse the myometrium) and causes them to go into prolonged constriction. The result is generalized ischemia and necrosis throughout the functional part of the endometrium. After several hours the constricted arteries open and blood again circulates into the functional zone. However, the weakened walls of the vessels rupture and blood leaks into the stroma where it forms lakes. The necrotic tissue sloughs into the uterine cavity together with blood from the ruptured arteries and from veins which are opened by the destructive processes.

The changes described above are well under way before bleeding is visible externally. As a rule they continue for several days since all regions of the endometrium do not bleed simultaneously. The destructive processes cause a considerable loss of tissue since most, if not all, of the functional layer is lost. Necrosis and bleeding cease and repair begins when the circulatory rate of the uterus is increased. This is brought about by an increase in the level of estrogenic hormone due, presumably, to the production of estrogen in the crop of follicles related to the next cycle.

In some instances menstruation occurs from an endometrium which is in the proliferative phase, i.e., one which has not entered the secretory phase. Such periods are called *anovulatory menstruation* since ovula-

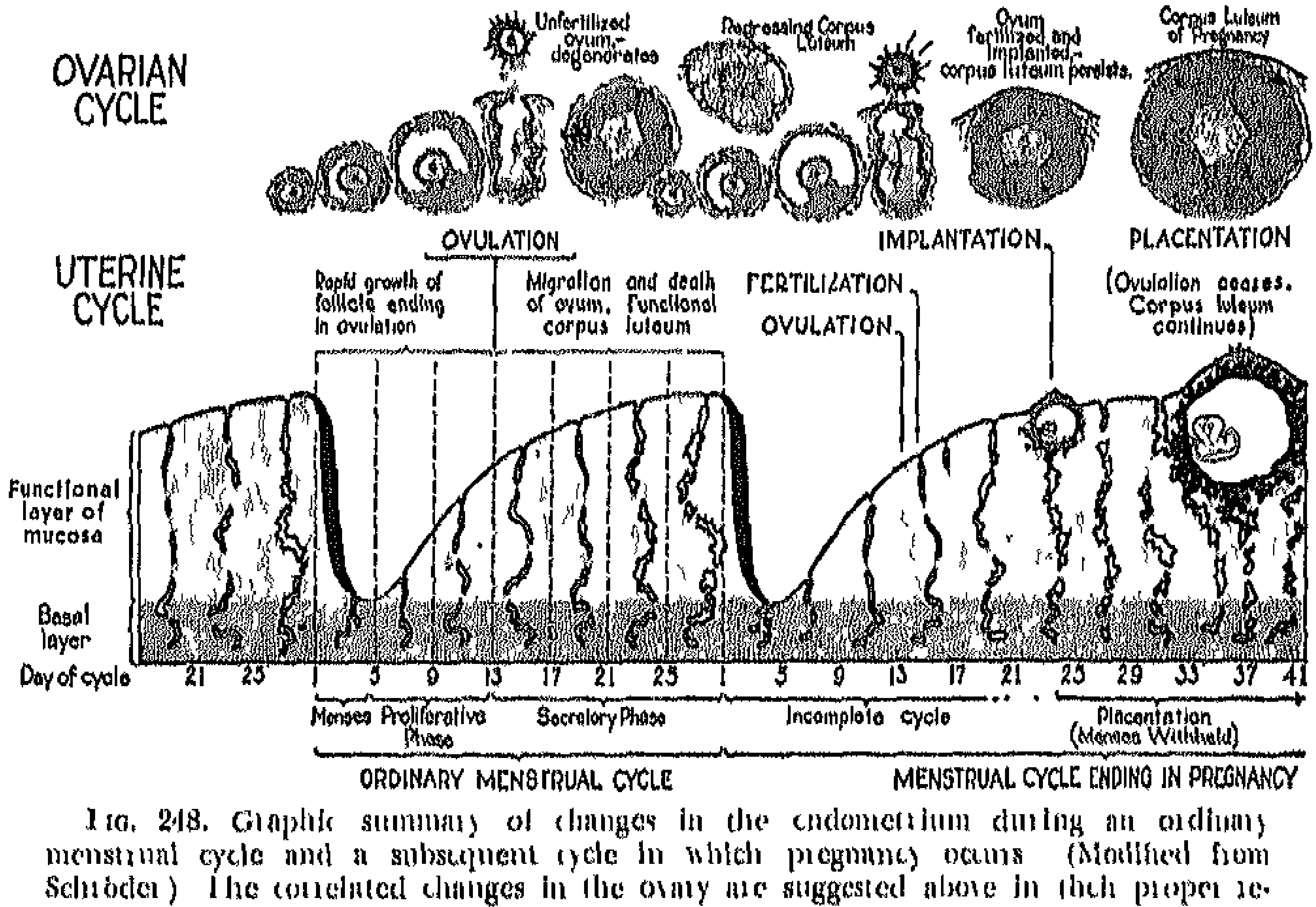

OVARIAN CYCLE
Unfertilized ovum-degenerates
Regressing Corpus Luteum
Ovum fertilized and implanted-corpus luteum persists.
Corpus Luteum of Pregnancy
OVULATION
IMPLANTATION
PLACENTATION
UTERINE CYCLE
Rapid growth of follicle ending in ovulation
Migration and death of ovum. Functional corpus luteum
FERTILIZATION
OVULATION
(Ovulation ceases. Corpus luteum continues)
Functional layer of mucosa
Basal layer
Day of cycle
21 25 1 5 9 13 17 21 25 1 5 9 13 17 21 25 29 33 37 41
Menses Proliferative Phase
Secretory Phase
Incomplete cycle
Placentation (Menses Withheld)
ORDINARY MENSTRUAL CYCLE
MENSTRUAL CYCLE ENDING IN PREGNANCY

Fig. 248. Graphic summary of changes in the endometrium during an ordinary menstrual cycle and a subsequent cycle in which pregnancy occurs (Modified from Schröder) The correlated changes in the ovary are suggested above in their proper relation to the same time scale. (Courtesy, Patten: "Human Embryology," Philadelphia, The Blakiston Company)

tion and corpus luteum have not occurred. In the absence of a corpus luteum, progesterone is not produced and the endometrium fails to develop beyond the proliferative phase. Such cycles are always sterile, since no ovum is released, and are usually shorter than *ovulatory* cycles, but not necessarily so. The steps leading to necrosis and bleeding are essentially the same in both types of cycles. Anovulatory cycles may occur in any woman and probably occur occasionally in all women, however, they are most common in girls during the first few years after *the onset of menstruation and in women entering the menopause.* This fact accounts for the relative infertility of girls and women during these phases of reproductive life.

The purpose of the menstrual cycle is the preparation of the uterine mucosa for the reception and implantation of the fertilized ovum. With the implantation of the ovum, the processes which are begun in the premenstrual stage are continued and by its growth in thickness and the increase in its blood supply, the mucosa becomes a part of the decidual structure which supports the embryo.

With the advance of age the thickness of the mucosa is greatly reduced, the glands become atrophied and disappear, although the deeper portions of some of the glands may become filled with a mucoid substance and remain as small cysts.

THE PLACENTA

The placentation of the fertilized ovum involves a number of changes in the structure of the uterus. Both the mucosa and muscularis increase in thickness. In the muscularis this increase is due to two factors: the growth of existing muscular elements, some of the fibers attaining a length of 500 microns, and to the addition of new muscle fibers. This increase in the thickness of the muscularis, which is quite marked in the early stages of pregnancy, is not quite so obvious in the later stages owing to the fact that it becomes thinner through stretching of the uterine wall.

The growth of the mucosa is the result of certain adjustments which provide for the nutrition of the embryo. The area in which these adjustments are made is known as the placenta. The first part of this change is essentially the same as that which occurs in the first stages of menstruation. The softened tissue is denuded of its epithelium and the supply of blood is increased through the enlargement of the vessels in the mucosa, the surface of which is thus prepared for the reception of the ovum.

The implantation of the ovum involves the attachment of the embryonic membranes to the wall of the uterus by the growth of processes *(chorionic villi)* from the chorionic vesicle into the softened tissue of the mucosa, which now becomes the *decidua*. The decidua is

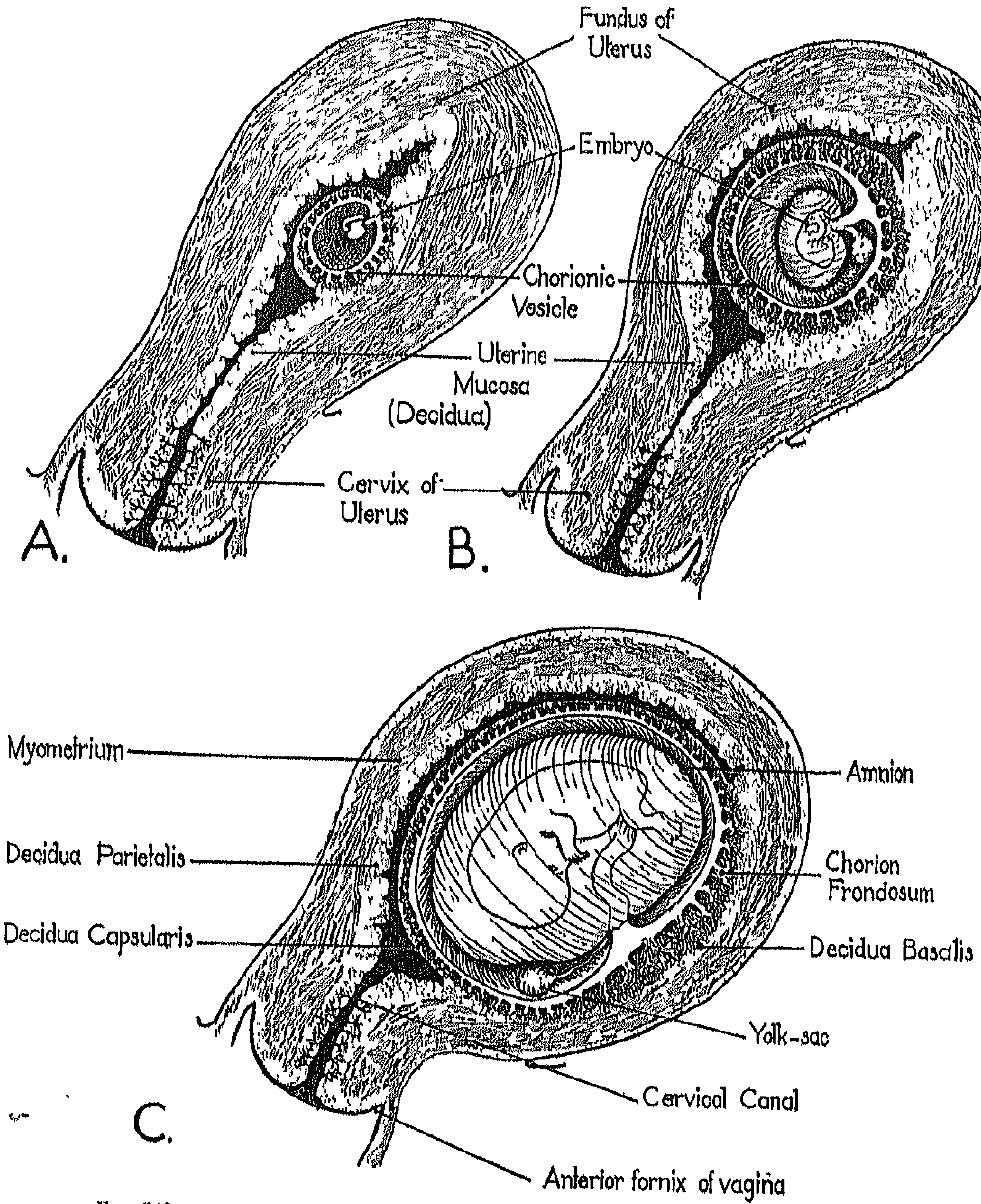


FIG. 249 Diagrams showing uterus in early weeks of pregnancy Embryos and their membranes are drawn to actual size. Uterus is within actual size range—about correct for a small primipara. (A) At three weeks. (B) At five weeks. (C) At eight weeks fertilization age. (Courtesy, Patten: "Human Embryology," Philadelphia, The Blakiston Company)

divided into three parts: the *decidua basalis*, which includes the portion of the uterine mucosa to which the chorionic villi are attached; the *decidua capsularis*, which spreads over the rest of the chorionic vesicle and for a time separates it from the cavity of the uterus: and the *decidua vera*, which includes the portion of the thickened mucosa that lines the remainder of the uterine cavity.

The chorionic villi consist of a central core of embryonic connective tissue covered by a layer of epithelium. During the early part of pregnancy this epithelial layer consists of both the cellular and syncytial trophoblast. The inner row of cells, called *Langhan's layer*, consists of cuboidal cells with lightly staining cytoplasm. The cell boundaries in this layer are distinct. External to this layer is a more deeply staining layer of cells known as the *syncytial layer*, in which the cell boundaries are indistinct. These cells show a brush border and their nuclei are scattered irregularly throughout the syncytium. Terminal branches of the umbilical arteries and veins extend into the connective tissue core of the villus. In the later stages of pregnancy (after the fourth month) the cells of Langhan's layer have almost entirely disappeared and the cells of the syncytial layer become more flattened. The blood vessels, which extend into the core of the villus, shift from a more central position in the villi of early pregnancy, to a more peripheral location in the villi of late pregnancy. Small clusters (knots and islands) of the trophoblast are present, either attached to the villi or lying free in the decidua basalis. In the early stages of pregnancy, new villi develop from these trophoblastic cell clusters. In later stages they decrease in size but some remain as cellular rests, although villi are no longer being formed. Evidence has accumulated indicating that the syncytial cells produce large amounts of progesterone and estrogenic hormone and that the cells of the cytotrophoblast produce chorionic gonadotrophin.

During the early stages of pregnancy, the chorionic villi become elongated and develop numerous branches, forming what is known as the *chorion frondosum*. The remaining surface of the chorion remains smooth, or loses any villi which may have been present, and becomes the *chorion laeve*. The chorion frondosum is in direct relation with the decidua basalis, while the chorion laeve lies in contact with the decidua capsularis. The decidua basalis constitutes the maternal, or uterine, portion and the chorion frondosum the embryonic portion of the placenta. As the villi grow into the decidua basalis, its substance is eroded and blood spaces are formed, the villi being located in these spaces. As the blood vessels are ruptured by the eroding process, the spaces are filled with the maternal blood which bathes the villi.

The chorionic vesicle enlarges with the growth of the embryo. The decidua capsularis becomes thinner by expansion and is pressed against

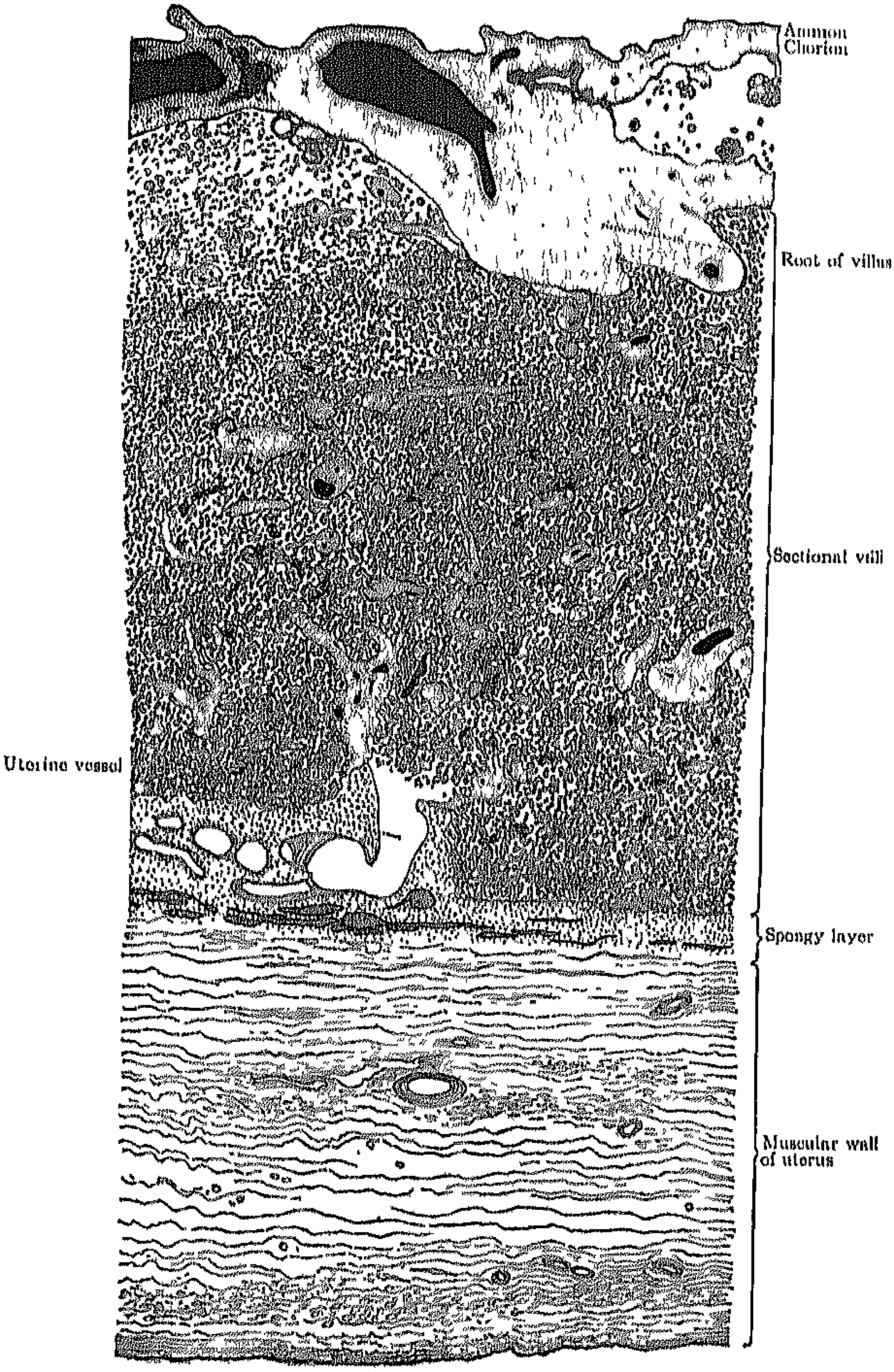


Fig. 250. Section through a normal placenta of seven months *in situ* (Minot). 5 ×.

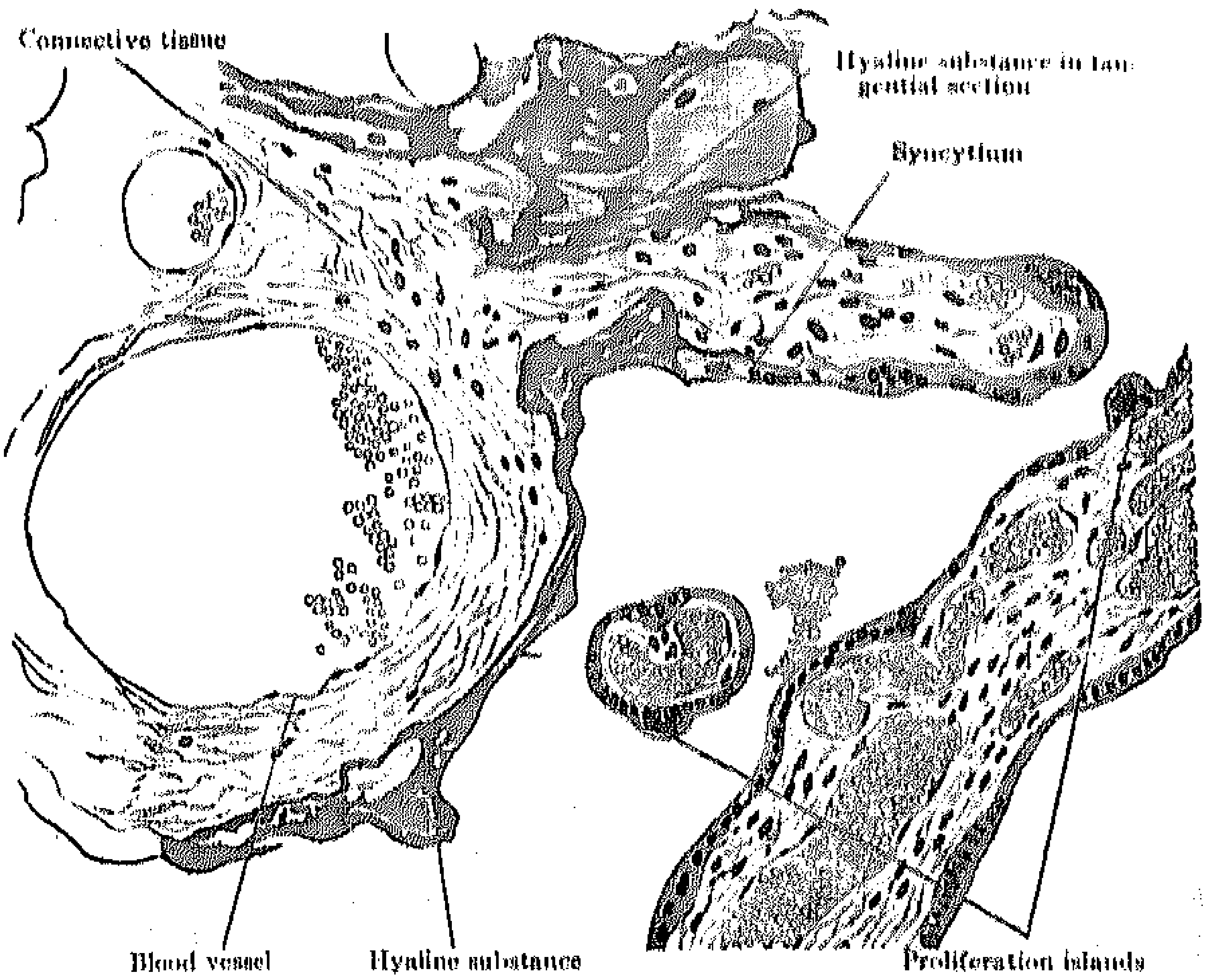


FIG. 251. From a section of a human placenta at term. 200 ×. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

the decidua vera, in which position it is finally resorbed. The chorion laeve and the decidua vera come together and eventually obliterate the uterine cavity. In the more superficial portion of the mucosa, the uterine glands undergo a process of degeneration, their epithelial cells forming a hyalinized mass in which slitlike clefts appear. The hyalin substance which forms from these masses is known as *canalized fibrin (fibrinoid).* The portions of the glands which remain in the deeper parts of the tissue, lose their epithelium and with the stretching of the uterine wall, become mere slits between the fibers. This forms an area of loose or spongy tissue in the zone in which the placental portion of the uterus splits off from the rest of the uterine wall when childbirth occurs.

The umbilical cord is attached to the placenta at, or near, the middle of the chorion frondosum. The subdivisions of the umbilical vessels are continued into the branches of the chorionic villi, in which the fetal blood comes into a relation with the maternal blood permitting the transfer between them of nutritive materials in one direction and of waste substances in the other. There is no direct communication between the maternal and fetal circulations, the transfer of materials from one to the other taking place through the agency of the cells which form the epithelium of the chorionic villi.

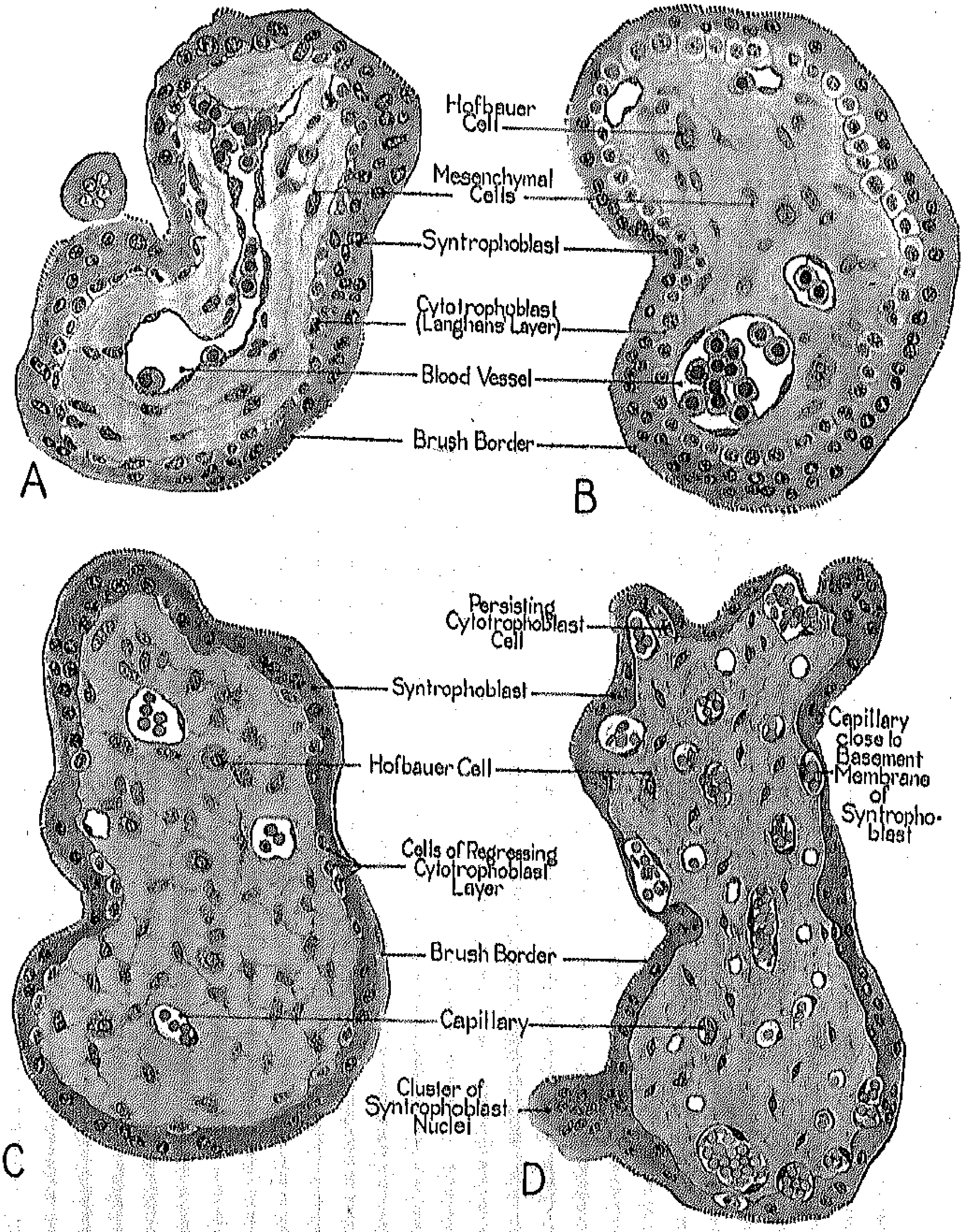

Hofbauer Cell
Mesenchymal Cells
Syntrophoblast
Cytotrophoblast (Langhans' Layer)
Blood Vessel
Brush Border
A
B
Persisting Cytotrophoblast Cell
Syntrophoblast
Hofbauer Cell
Cells of Regressing Cytotrophoblast Layer
Brush Border
Capillary
Cluster of Syntrophoblast Nuclei
Capillary close to Basement Membrane of Syntrophoblast
C
D

FIG. 252. Chorionic villi at various ages. (Camera lucida drawings 350 ×.) (A) From chorion of four-week embryo (C-R 4.5 mm.). (B) Chorion from an embryo of about six and a half weeks (C-R 15.1 mm.). (C) Placenta from a fetus of the fourteenth week. (D) Placenta at term. (From preparation loaned by Dr. Burton L. Baker in Patten: "Human Embryology," Philadelphia, The Blakiston Company.)

THE VAGINA AND THE FEMALE URETHRA

THE VAGINA. The vagina is a muscular, tubelike structure, flattened in the anteroposterior direction, which lies below and communicates with the uterus. Its wall consists of a *mucosa*, a *submucosa*, a *muscularis,* and a *fibrosa*. The mucosa includes a stratified squamous epithelium and a layer of delicate fibrous tissue, in which both lymphocytes and a few granulocytes are present. Occasionally the lymphocytes are in the form of small nodules. This layer is usually referred to as a *tunica propria*. Numerous tall papillae from the tunica propria penetrate the deep surface of the epithelium. The submucosa is considerably thicker, and consists of coarse fibers, both collagenous and elastic.

After puberty the thickness of the epithelial layer varies with the menstrual cycle. At the approach of the period, the epithelium increases in thickness and appears to consist of three parts: a basal or germinal portion, a middle, dark, cornified portion, and a superficial portion which is described as the functional layer.

The cells of the cornified layer are fusiform and contain elongated nuclei and basophilic granules which give the layer its dark appearance. During menstruation, the functional layer and a part of the cornified

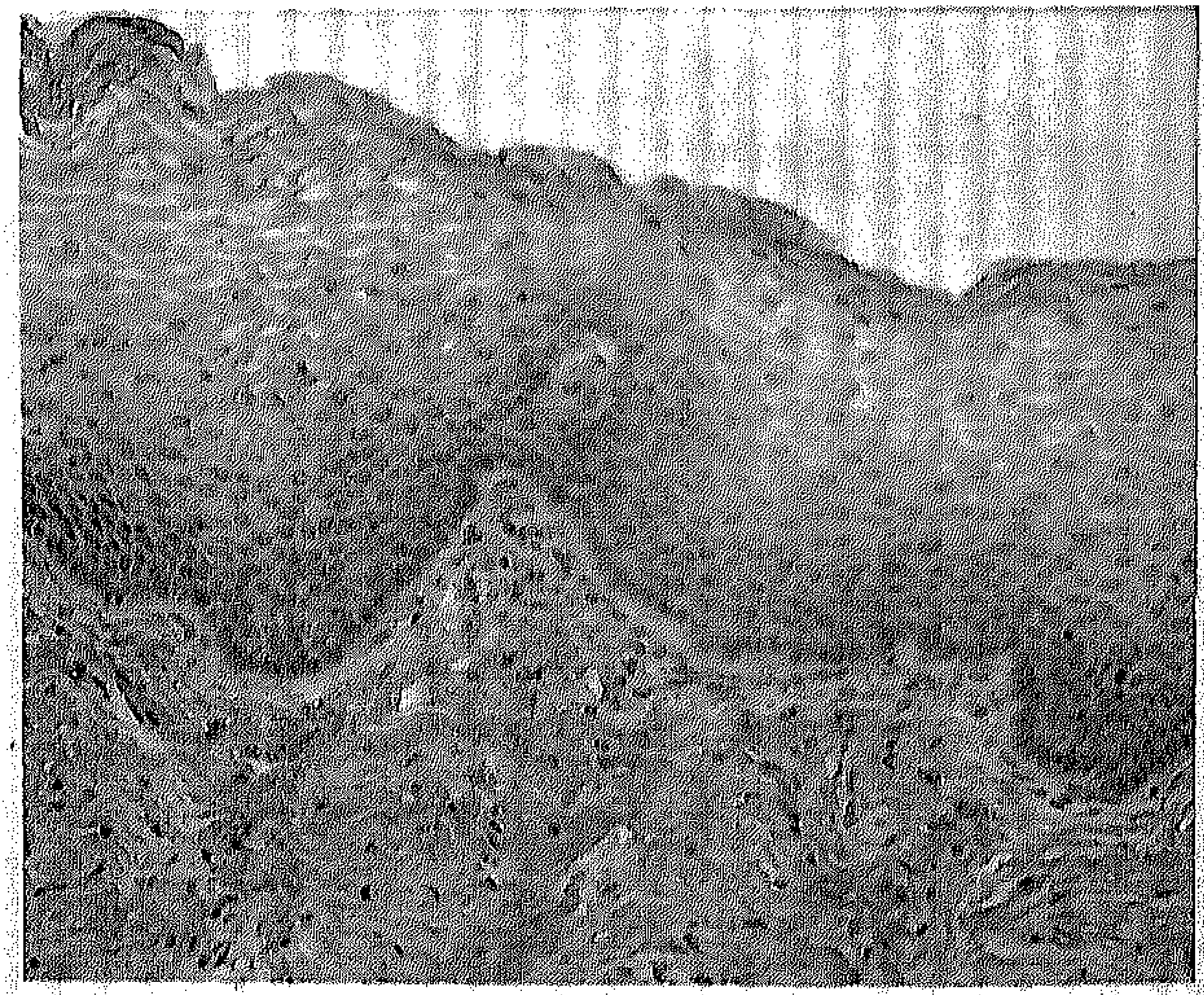


FIG. 253. Section through the mucosa of human vagina. Photomicrograph.

layer may be more or less completely desquamated; their restoration, after active menstruation has ceased, resulting from the proliferation of cells from the germinal layer.

The submucosa and mucosa are raised into large folds, the *columnae rugae*. The fibrous tissue which supports these folds is penetrated by numerous, thin-walled veins which give it the general appearance of erectile tissue. Although it possesses no glands, the inner surface of the vagina is moistened by a mucoid, slightly acid secretion. The pH of the vagina is lowest during the late proliferative phase of cycle, due to the high level of estrogen at that time. Estrogen is related to the production of glycogen in the vaginal mucosa and the action of lactic acid forming bacteria (Döderlein's bacilli) upon the glycogen results in a drop in the pH of the vaginal fluid.

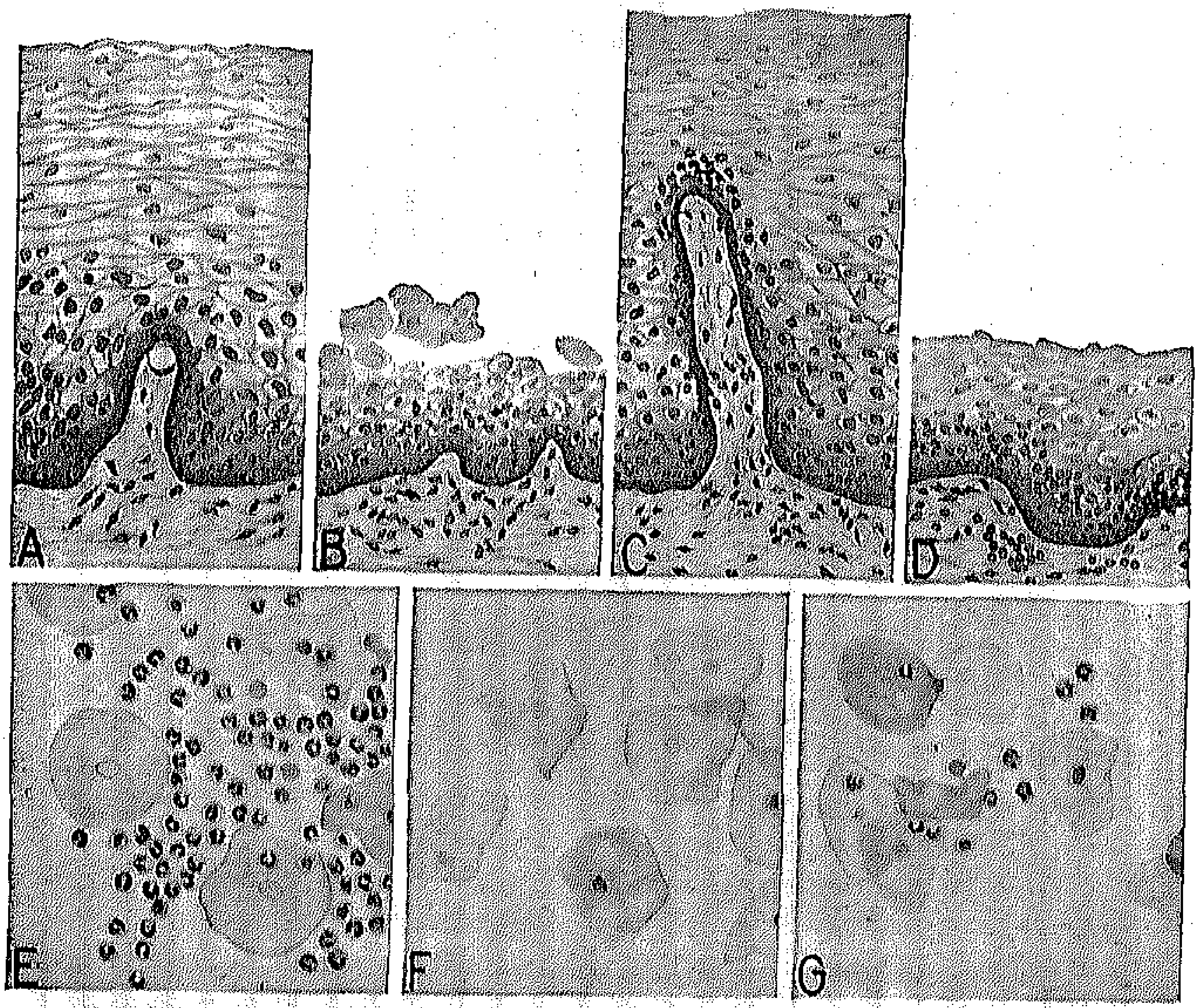


FIG. 254. Vaginal changes occurring under influence of estrogenic hormone. (A—D) Sections of vaginal epithelium. 200 ×. (A) Newborn. (B) Infant of two weeks. (C) Sexually mature adult. (D) Senile. (E—F) Vaginal smears from adult at different times in the ovulatory-menstrual cycle. (Redrawn after Papanicolaou. Am. J. Anat., Vol. 52, Suppl., 1933.) (E) Shortly after cessation of menstruation. (F) At about the time ovulation is due to occur. (G) Shortly after ovulation. (Courtesy, Patten: "Human Embryology," Philadelphia, The Blakiston Company.)

The muscularis lies external to the submucosa. It consists for the most part of longitudinally directed smooth muscle fibers. Circular fibers are intermingled with the longitudinal fibers in the inner portion. *The muscle layers of the vagina are continuous with those of the uterus.* At the introitus the vaginal wall contains striated muscle.

External to the muscularis is a layer of coarse, rather closely interwoven, collagenous and elastic fibers. This tissue constitutes the fibrosa, which merges into the more loosely arranged surrounding connective tissue that supports the vagina by attaching it to adjacent structures.

The vaginal opening is partially occluded by a fibrous membrane, the *hymen*. This membrane is richly supplied with blood vessels and is covered by a continuation of the epithelial lining of the vaginal canal.

The blood supply is by vessels which form a network between the mucosa and the muscularis. Some of the branches from this network pass to the fiber bundles of the muscularis which they supply, while others enter the mucosa and form a vascular plexus beneath the epithelium. The veins arise from the plexuses and pass from the wall of the vagina, their course being parallel with the vaginal canal.

The lymphatics consist of capillary plexuses in the mucosa, the muscularis and the fibrosa, from which the efferent vessels take their origin.

The nerves are mainly from the autonomic system, their fibers being associated with small ganglion cells which send processes to the walls of the blood vessels and to the muscles. Sensory fibers enter the mucosa where they end in relation to special sense organs. In all probability, some of the sensory fibers end in association with the cells of the epithelium.

The changes which take place in the vaginal mucosa at different stages of the menstrual cycle are indicated by the number and character of the free cells in the desquamated tissue. These may be studied in vaginal smears, from which the different stages in the ovarian cycle can be estimated with considerable accuracy in some of the lower animals. In the human subject changes are somewhat less clear-cut, but they too may be followed and interpreted by an experienced observer.

The vagina is separated from the rectum by a sheet of fibroelastic tissue, in which scattered bundles of smooth muscle fibers are present. This forms the *rectovaginal septum*. A similar sheet of tissue lies between the vagina and the urethra, the *urethrovaginal septum*.

THE FEMALE URETHRA. The urethra is much shorter in the female than in the male. Its mucosa consists of an epithelium resting on a stroma of fibroelastic tissue, which contains many thin-walled, venous spaces. The small, irregular bundles of smooth muscle tissue, which appear between these spaces, gives this portion of the urethral wall the appearance of the erectile tissue of the male corpus spongiosum, with which this portion of the female urethra is homologous. Glands

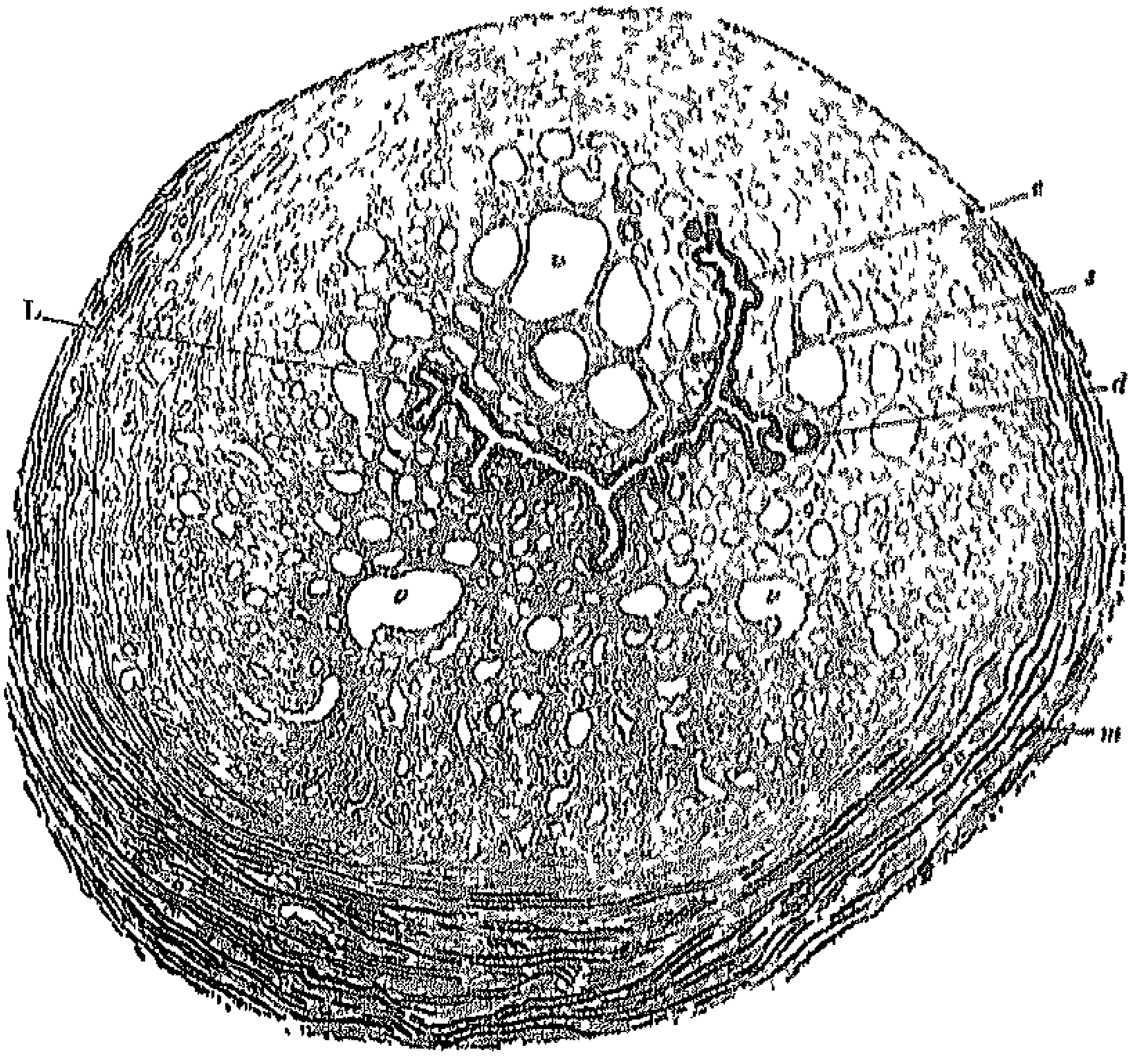


FIG. 255. Cross section of the female urethra (Koelliker). *(d)* Gland-like diverticulum *(e)* Epithelium. *(L)* Lumen of the urethra. *(m)* Striated muscle. *(s)* Corpus spongiosum, containing venous spaces *(v)* and smooth muscle (Courtesy, Bremer-Weatherford: "Text book of Histology," Philadelphia, The Blakiston Company.)

similar to the glands of Littré in the male open into small, epithelial crypts formed by depressions of the urethral epithelium.

The transitional epithelium of the bladder is continued into the upper part of the urethra. Its lower portion is lined by a stratified squamous epithelium which is continued into it from the vestibule. The epithelium which lines its intermediate portion may be stratified columnar, pseudostratified, or even simple columnar.

The muscularis consists of circular and longitudinal layers. The circular fibers unite with those of the bladder wall to form a sphincter muscle about the internal urethral opening. At its lower end the urethra is enclosed by the striated fibers of the sphincter muscle of the vagina. Its intermediate part, in the deep perineal space, is surrounded by the striated fibers of the sphincter urethrae muscle.

EXTERNAL FEMALE GENITALIA

The external structures of the female genitalia are the *labia majora,* the *labia minora,* and the *clitoris.* The labia majora are thick folds of skin supported by connective tissue in which a large amount of fat is present. Numerous hair follicles, with sweat and sebaceous glands, are present on the outer surfaces of these folds. The integument, covering the medial surfaces, is more delicate and contains fewer hairs and glands. The connective tissue beneath the skin contains bundles of smooth muscle fibers, forming a layer known as the *tunica dartolabialis*.

The labia minora (*nymphae*) are continuous with the labia majora at their base, but are separated otherwise by a deep furrow, the *interlabial groove*. The minor folds are covered by an integument which contains a number of small sebaceous glands. Hair follicles and sweat glands are absent. These folds are supported by a loose, fibroelastic tissue which, together with the integument by which their medial surfaces are covered, is continuous with the mucous tissue of the *vestibule*, or space enclosed by the labia.

The clitoris is the homologue of the penis. It consists of two bodies of erectile tissue which bear a close resemblance to the corpora cavernosa of the male organ. The corpus spongiosum is divided by a cleft and forms the *bulbus vestibuli*.

THE GLANDS OF BARTHOLIN

In the female, the glands of Bartholin correspond to the bulbourethral glands in the male. They are small tubuloacinar glands, located on either side of the vaginal opening. They are lined by columnar cells which produce a whitish, mucoid secretion. The glands are divided into lobules by thin, fibromuscular septa. The ducts from the lobules unite to form a single excretory duct for each gland. The excretory duct is lined by columnar cells, except at its outlet where the epithelium is stratified columnar.

22

The Eye

The eye is the organ of vision. It consists of the eyeball, or *ocular bulb (bulbus oculi),* and its associated structures: the *eyelids,* the *lacrimal apparatus, fascia,* the *conjunctiva* or mucous membrane of the eye, and the *ocular muscles.*

The ocular bulb is an almost spherical structure occupying a large cavity, the *orbit,* in the anterior aspect of the cranium. In appearance, the eyeball seems to be formed by portions of two spheres of unequal size; the larger sphere forming the posterior four-fifths of the eyeball while the smaller one forms the anterior one-fifth. The structures of these two, however, are continuous. The central point of the anterior sphere is known as the *anterior pole* of the eye. A corresponding central point on the posterior segment is called the *posterior pole.* The *optic axis* is a line joining these two poles. Circles drawn around the circumference of the eye so as to pass through both the anterior and the posterior poles form the *meridians.* The *equator* is the circle which would divide the eye into anterior and posterior portions equal distances from the anterior and posterior poles. The *visual line* or *axis* (which is of clinical importance) is the line which connects the external object (being observed) with the fovea centralis (area of most acute vision). The eyeball is attached to the walls of the orbit by fibrous ligaments and by the ocular muscles. The space between the bulb and the wall of the orbit is occupied by a mass of fatty tissue which forms a cushion on which the bulb rests. The anterior part of the eyeball is exposed, except for a small portion which is covered by the eyelids.

The eyelids are curtainlike folds of the integument which are located in front of the ocular bulb and can be drawn over it for protection.

The lacrimal apparatus consists of the *lacrimal gland,* which produces a watery secretion serving to keep the anterior or exposed surface of the eyeball moist, and the *lacrimal sac* and *ducts* that convey the secretion from the gland to the surface of the eye.

Interposed between the orbital fat and the ocular bulb is a thin, fibrous membrane known as the *ocular fascia* or *capsule of Tenon.* This fascia begins at the optic nerve and passes forward, between the orbital fat and the sclera, to a point just anterior to the attachment of the ocular muscles. Anteriorly it is continuous with the conjunctiva. This ocular fascia is closely applied to the sclera and tendons of the ocular muscles by means of fine strands of reticular tissue. The communicating spaces thus formed between the fascia and the scleral coat of the bulb are known as the *episcleral space* or *space of Tenon* and contains a lymph-like fluid. The ocular muscles pierce the fascial capsule as they pass to

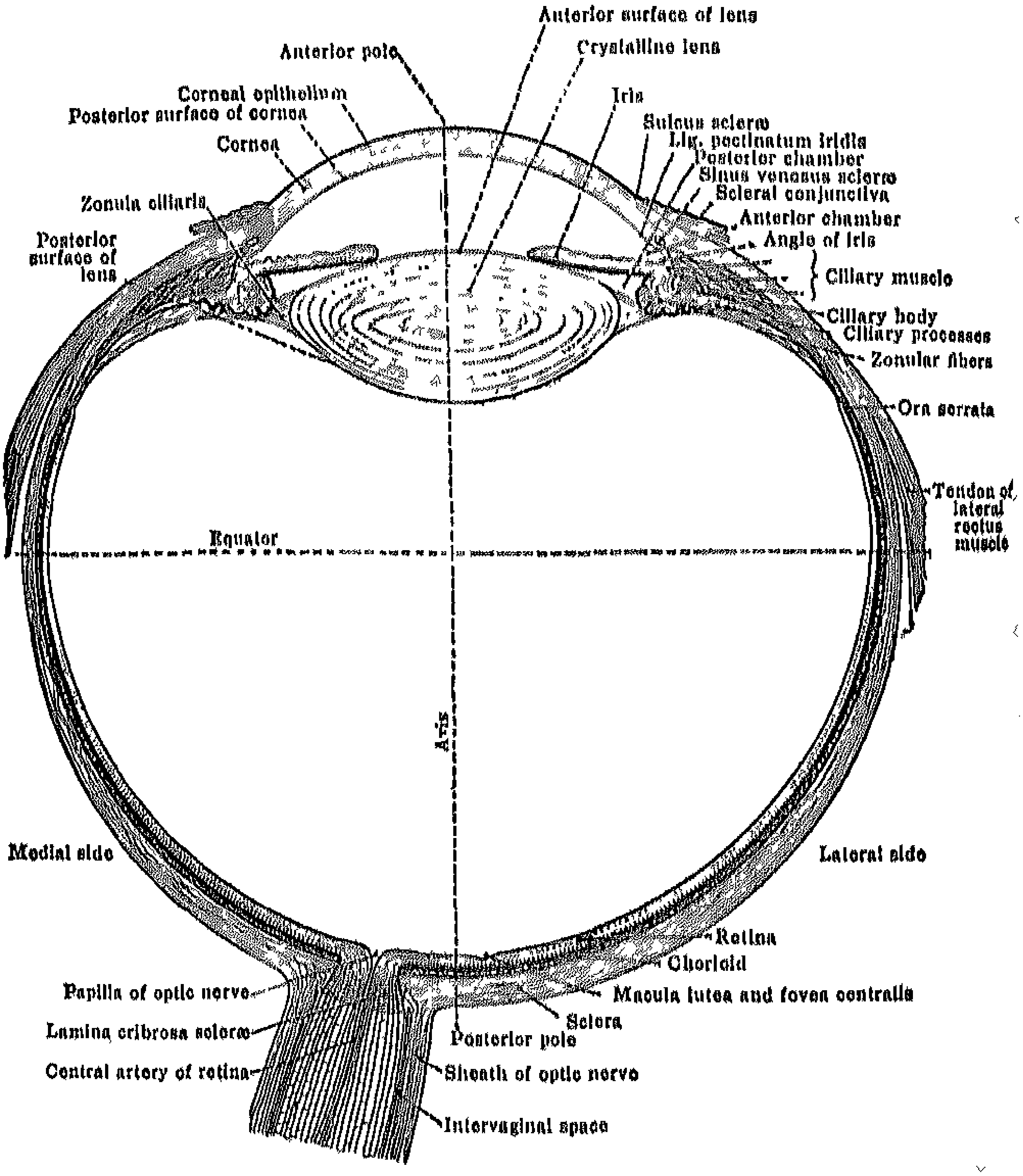


FIG. 256. Schematic horizontal meridional section of right eye. 4 ×. (Courtesy, J. Parsons Schaeffer, Ed.: "Morris' Human Anatomy," Philadelphia, The Blakiston Company.)

the outer or scleral coat of the eyeball. Tubular extension of the bulbar fascia is reflected on and encloses approximately the anterior one-half of each ocular muscle.

The conjunctiva or mucous membrane of the eye covers the anterior portion of the eyeball and is reflected over the inner surfaces of the eyelids.

The ocular muscles move the eyeball within the orbit and help in bringing the eyes into focus on an object.

THE EYEBALL

The eyeball *(bulbus oculi)* is only approximately spherical. Its greatest diameter is in the anteroposterior direction, being slightly less than an inch. Its other diameters are less, due to the fact that it is slightly flattened from above downward and also from side to side.

The eyeball consists of three concentric layers, or tunics. The most external of these is the sclera, which is called the *fibrous coat (tunica fibrosa).* Anteriorly it consists of the transparent *cornea* which includes approximately one-fifth of the outer part of the eyeball and the white, opaque and densely fibrous part which includes the remaining four-fifths of the outer coat that constitutes the *sclera.* The visible part of the sclera which surrounds the cornea is known as the "white" of the eye. Along its anterolateral surface the sclera affords attachment for the ocular muscles. Posteriorly the sclera is perforated by the fibers of the optic nerve. The portion of the external coat through which the optic nerve emerges is known as the *lamina cribosa.*

The middle layer is known as the *vascular coat (tunica vasculosa)* and contains a good deal of pigment. In the posterior three-fourths of the eyeball, the vascular coat is called the *choroid.* As it extends anteriorly, it forms the *ciliary body* and *iris* (smooth muscle fibers are present in both of these structures). The ciliary body includes the *ciliary muscle* or *muscle of accommodation,* which by its contraction, relaxes the pull of the fibers of the suspensory ligament and releases their tension on the capsule of the lens, thus permitting a change in its curvature and a sharper focus of the image on the retina. The iris is a fold of the ciliary body, which hangs in front of the lens like a curtain. A circular aperture approximately in the middle of the iris is known as the *pupil* while the portion of the iris which bounds the pupil is known as the *pupillary border.* The diameter of the pupil is increased or decreased by the action of the iridial muscles.

The innermost coat or *retina (tunica nervosa)* is composed of two layers, an outer layer which is nearer the surface of the eyeball and an inner layer which is nearer the vitreous humor. The outer layer is a pigmented layer, while the inner layer is made up of nervous elements that are characterized by their sensitivity to light. It is this layer which receives the impressions of the images that are imposed on it in vision. The retina loses its visual elements in a zone known as the *ora serrata*, anterior to which it continues as a two layered, epithelial structure in which the cells are deeply pigmented. This pigmented nonvisual portion of the retina extends forward on the inner surfaces of the ciliary body and the iris. The fibers of the optic nerve leave the eyeball at a point slightly medial (about 3 mm.) to the posterior pole. This area which has neither rods nor cones (receptor cells for vision) is called the *optic disc* or the *blind spot* of the eye. Slightly lateral to the posterior pole is a slightly raised, yellowish area called the *macula lutea*. A small depression in the center of the macula is known as the *fovea centralis*. This is the point of the most acute vision and contains only cones.

The eye is divided into two segments, posterior and anterior. The anterior segment is again divided into two chambers, anterior and posterior.

The larger sphere forms the posterior segment of the eye and its structures are adapted to the reception and transmission of visual images. Its outer coat is opaque and allows no light to enter. It is separated from the anterior segment by the lens and the suspensory ligament. It contains a jellylike substance known as the *vitreous body*, which is pierced by a tubelike channel, the *hyaloid canal*, that extends from the point where the fibers of the optic nerve converge (optic disc) to the posterior surface of the lens. This canal provides for the passage of the fetal hyaloid artery. The vitreous body is separated from the inner surface of the retina by a thin, cuticular membrane known as the *hyaloid membrane*.

The space between the lens, suspensory ligament and the cornea is the anterior segment of the eye. The anterior chamber of the anterior segment is bounded in front by the cornea and behind by the iris. The anterior chamber communicates through the pupillary opening with the posterior chamber which is the space between the iris and the lens with its attached suspensory ligament. Both the anterior and posterior chambers of the eye are filled with a fluid known as the *aqueous humor*.

THE POSTERIOR SEGMENT OF THE EYE

The wall of the ocular bulb (eyeball) in its posterior division includes: (1) the *sclera*, (2) the *choroid*, and (3) the *retina*.

1. THE SCLERA. The sclera is a layer of densely compacted, fibrous tissue forming the external layer of the eyeball. It is approximately 1 mm. in thickness about the optic nerve, but becomes thinner toward the equator, being about 0.4 mm. in thickness just posterior to the insertion of the ocular muscles. Anterior to this its thickness increases to about 0.6 mm.

Where the fibers of the optic nerve pierce the sclera, it is perforated

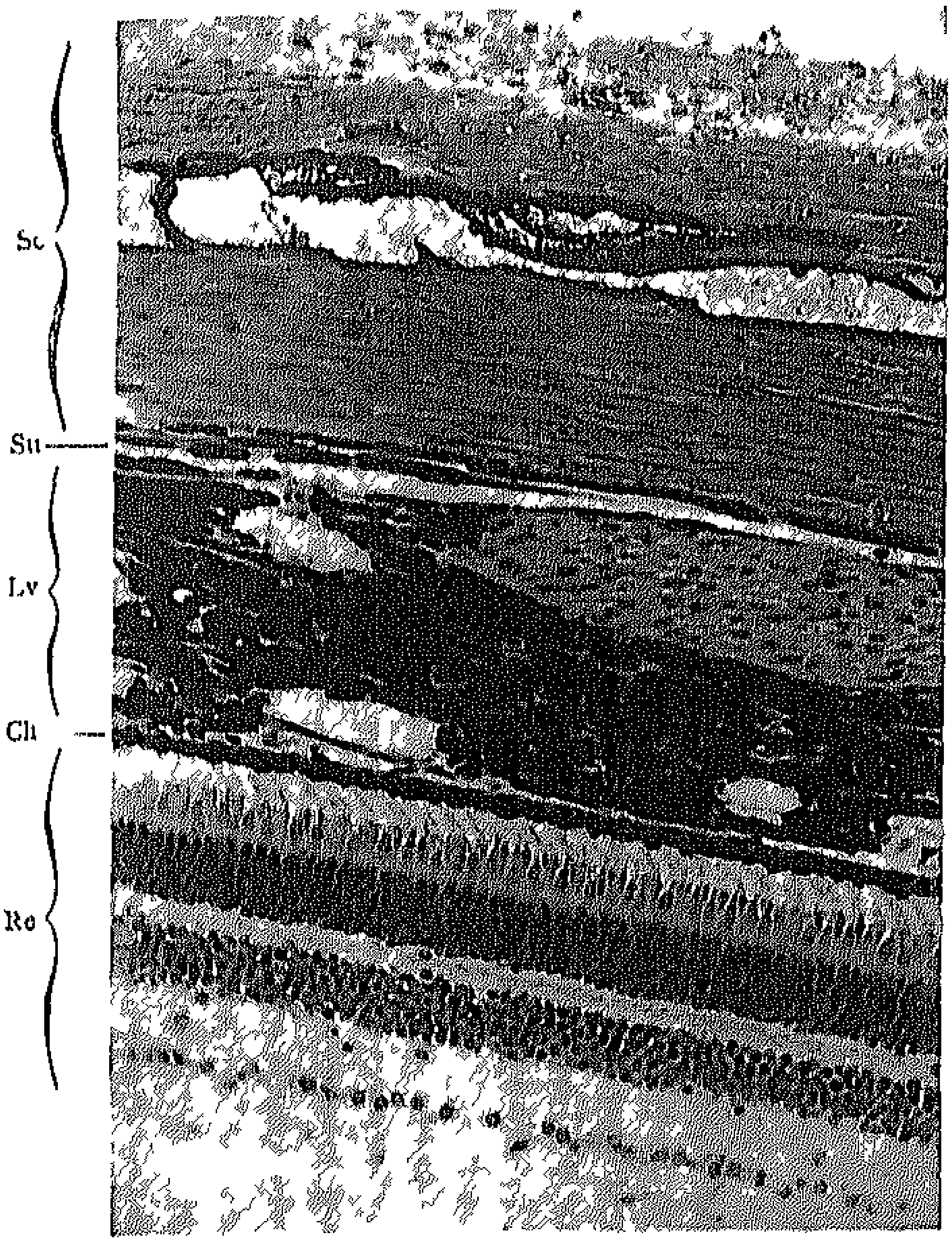


Fig. 257. Section through the posterior segment of the eyeball (Sc) Sclera. (Su) Suprachoroid. (Lv) Lamina vasculosa. (Ch) Chorio capillaris. (Re) Retina Photomicrograph

by numerous small openings; because of this the area is called the *lamina cribrosa*. The junction of the two spheres of unequal size produces a depression or furrow on the eyeball known as the *scleral sulcus*. The anterior extent of the sclera forms a V-shaped depression into which the tapered end of the cornea fits. The inner wing of the V (called the *scleral spur*) gives attachment to the ciliary body.

The sclera is composed of an outer *fibrous layer* and an inner layer called the *lamina fusca*.

The outer fibrous layer consists of a dense meshwork of collagenous fibers among which are scattered elastic fibers. The fibers are arranged in the form of flattened, lamellated bundles, the direction of which is both meridional (longitudinal) and equatorial (transverse). Flattened, irregularly stellate cells with anastomosing processes are present in the spaces between the fiber bundles.

The inner layer of the sclera (lamina fusca) is characterized by i brownish color. It consists of smaller bundles of collagenous fibers inte spersed with more elastic fibers and pigment cells which fill the inte fibrillar spaces and gives the layer its brownish color. A narrow spa between the lamina fusca and the choroid is known as the *suprachoro space*. This space is crossed by a number of fibrous trabeculae and h been described as being lined by a delicate layer of endothelium. The is considerable doubt whether the suprachoroid space is to be regard

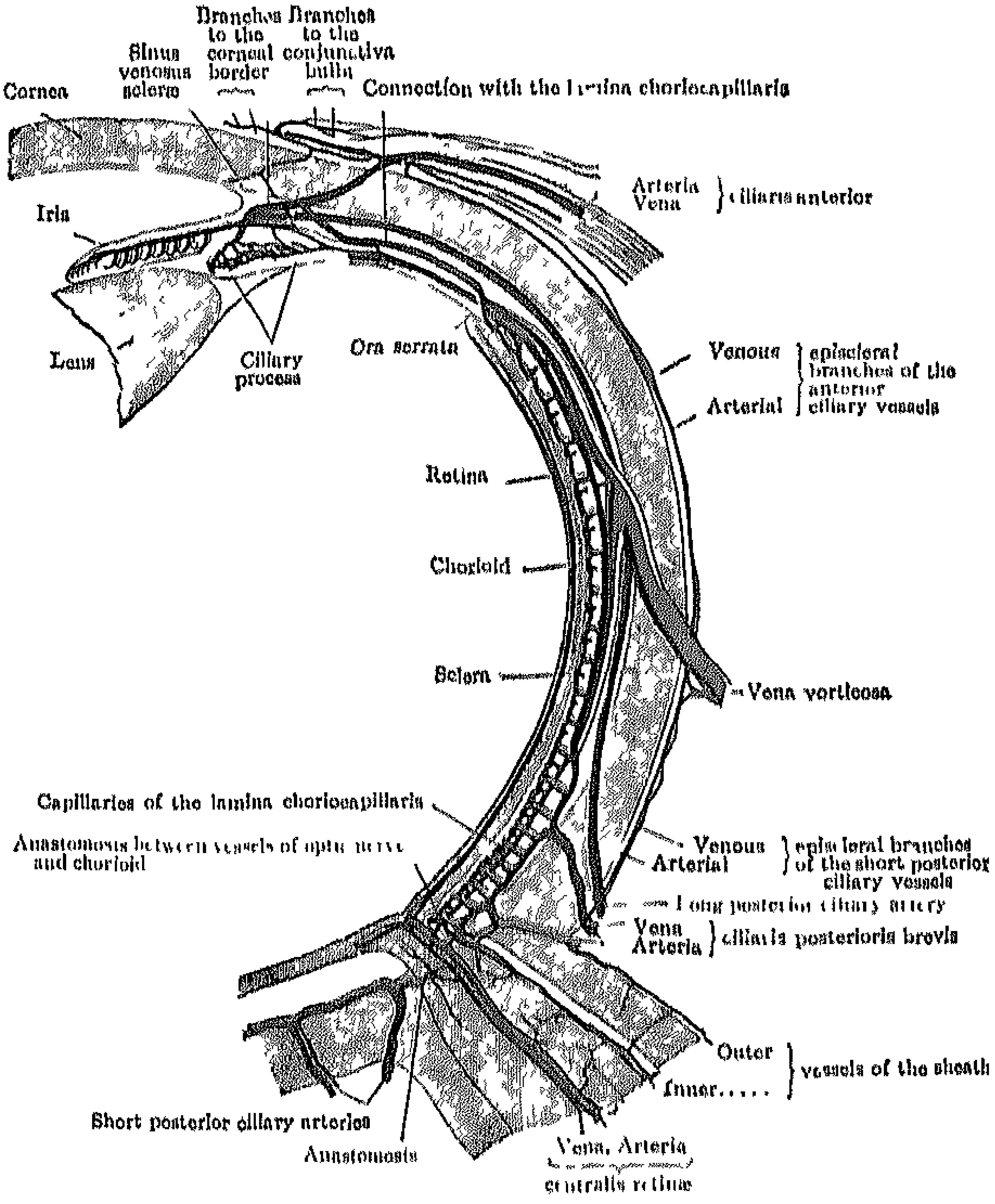

Branches to the corneal border
Branches to the conjunctiva bulbi
Sinus venosus sclerae
Cornea
Connection with the lamina choriocapillaris
Iris
Arteria
Vena
ciliaris anterior
Lens
Ciliary process
Ora serrata
Venous
Arterial
episcleral branches of the anterior ciliary vessels
Retina
Chorioid
Sclera
Vena vorticosa
Capillaries of the lamina choriocapillaris
Anastomosis between vessels of optic nerve and chorioid
Venous
Arterial
episcleral branches of the short posterior ciliary vessels
Long posterior ciliary artery
Vena
Arteria
ciliaris posterioris brevis
Outer
Inner.....
vessels of the sheath
Short posterior ciliary arteries
Anastomosis
Vena, Arteria
centralis retinae

FIG. 258. Diagram of the ocular blood vessels drawn into a horizontal section of the le eye. (From Stöhr, after Leber) (Courtesy, J. Parsons Schaeffer, Ed.: "Morris' Huma Anatomy," Philadelphia, The Blakiston Company)

as a definite lymph space, since in all probability, the presence of an endothelium is doubtful.

Externally the sclera is covered by a layer of loose connective tissue which is richly supplied with blood vessels. This layer is interposed between the tissue of Tenon's capsule and the sclera. Anteriorly it becomes continuous with the subepithelial tissue of the sclera conjunctiva.

The blood supply to the sclera is by branches of the ciliary vessels which pass through it on their way to the choroid. The veins are tributary to the anterior and posterior ciliary veins.

There are no lymphatics.

The ciliary nerves send branches which supply the sclera.

2. THE CHOROID. The choroid or vascular tunic, lies between the sclera and the retina. It extends from the area about the optic nerve to the ora serrata, anterior to which it soon changes to the muscular structure of the ciliary body. The choroid is considerably thinner than the sclera. In the region of the optic nerve it has a thickness of about 0.2 mm., and gradually decreases to a thickness of 0.1 mm. or less at the ora serrata where it loses its vascular character.

The choroid consists of four layers: the *lamina suprachoroidea,* which lies immediately within the lamina fusca of the sclera; the *lamina vasculosa,* or choroid proper, which is the thickest and most important part of the vascular tunic; the *lamina choriocapillaris;* and the *lamina basalis.*

The lamina suprachoroidea presents essentially the same structural features as the lamina fusca. It consists of interlacing bundles of collagenous and elastic fibers and is separated from the lamina fusca by a narrow cleft (as seen in sections), the suprachoroidal space. In the living, it is probable that the lamina suprachoroidea of the vascular tunic and the lamina fusca of the sclera constitute a single layer consisting of bundles of connective tissue, the interfibrillar lymph spaces being lined by a delicate endothelium. In fixed material, the shrinkage of the tissues causes the bundles to separate, the space which is formed between them being crossed by delicate fibrous trabeculae. The interfibrillar spaces in both layers are occupied by numerous large, irregularly branched connective tissue cells which are filled with granules of a dark-brown pigment known as *melanin.* Cells of this type are called *chromatophores.*

Anterior to the equatorial region of the eyeball the choroid contains a number of small bundles of smooth muscle fibers. The manner in which these bundles are arranged gives them a stellate appearance, for which reason they are commonly referred to as *muscle stars.*

The lamina vasculosa or choroid proper is characterized by the presence of numerous blood vessels. The larger vessels, most of which are venous, are located in the outer portion of the layer. The inner portion is occupied by the smaller vessels. The connective tissue between the blood vessels is more compactly arranged than in the suprachoroidea and contains fewer chromatophores. Numerous nonpigmented connective tissue cells are found around the blood vessels.

The blood supply of the choroid is by branches from the short ciliary arteries. The veins form the large vessels previously referred to, which converge in a peculiar "whorled" formation and are known as the *venae vorticosae*

The lamina choriocapillaris *(membrane of Ruysch)* is a thin layer made up of a delicate meshwork of collagenous and elastic fibers in which are found numerous capillaries. These vessels, which form a wide-meshed network arranged in one plane, are characterized by their unusually large caliber, a condition especially noticeable in the region of the macula. Around the area of the fovea centralis the capillary network is very dense. This layer does not extend anteriorly beyond the ora serrata and therefore does not contribute to the formation of the ciliary body.

In some of the lower animals a thick, wavy layer of closely interwoven collagenous fibers is interposed between the vascular and capillary layers, and reflects light in such a way that the eye has a peculiarly luminous appearance. This layer is known as the *tapetum*. A layer of this type occurs in the eyes of the herbivorous animals, the *tapetum fibrosum*. A similar effect is produced in the eyes of the carnivorous animals by the presence of a cellular layer of some depth, the reflection of the light being due to the number of minute crystals which the cells contain. In these animals the layer is called the *tapetum cellulosum*.

The lamina basalis *(membrana vitrae; membrane of Bruch)* is the innermost layer of the choroid. It is a thin homogeneous layer that lies between the choriocapillaris and the pigmented layer of the retina. It consists of two parts: an outer portion formed by the condensation of a thin layer of elastic fibers (outer elastic layer) and an inner homogeneous layer. This layer is regarded by some as a cuticular layer belonging to the pigmented layer of the retina.

The ciliary nerves send branches into the stroma of the suprachoroid and choroid. Here, these branches form a plexus which lies in relation to groups of ganglion cells, the fibers of which pass to the walls of the blood vessels. Cells of this type are also to be found in relation to the vessels about the canal of Schlemm. There are no sensory fibers in the choroid.

3. THE RETINA. The retina *(pars nervosa)* is a layer composed almost entirely of nervous elements. It lines the entire inner surface of the bulbus oculi from the optic disc to the pupillary border of the iris. It has three divisions: the first or visual portion, contains the elements which are sensitive to light and is known as the *pars optica*, the second

lies on the inner surface of the ciliary body and is known as the *pars ciliaris,* and the third part forms the inner or posterior layer of the iris and is known as the *pars iridica.*

The visual portion of the retina extends anteriorly from the optic disc and ends somewhat abruptly, by the cessation of its visual elements, in an irregular line close to the border of the ciliary body. The irregular line where this change in the structure of the retina takes place is known as the *ora serrata.*

The retina presents the *macula lutea,* a thickened oval area, yellowish in color, about 3 mm. lateral to the optic disc. A small depression in the center of the macula is known as the *fovea centralis.* The fovea is the point of most acute vision and is located at the posterior end of the visual axis. The *optic disc* is a small area about 1.5 mm. in diameter, upon which the retinal fibers converge to pass out of the eyeball as the optic nerve. Since this area is not supplied with visual elements, it forms the "blind spot" of the retina.

The supporting structures of the retina are modified neuroglial elements known as the fibers of Müller. These fibers pass through the retina from its inner surface to the level of the basal portions of the rods and cones. Their inner extremities form expansions which join together to form the *inner limiting membrane* lying between the fiber layer and the hyaloid membrane.

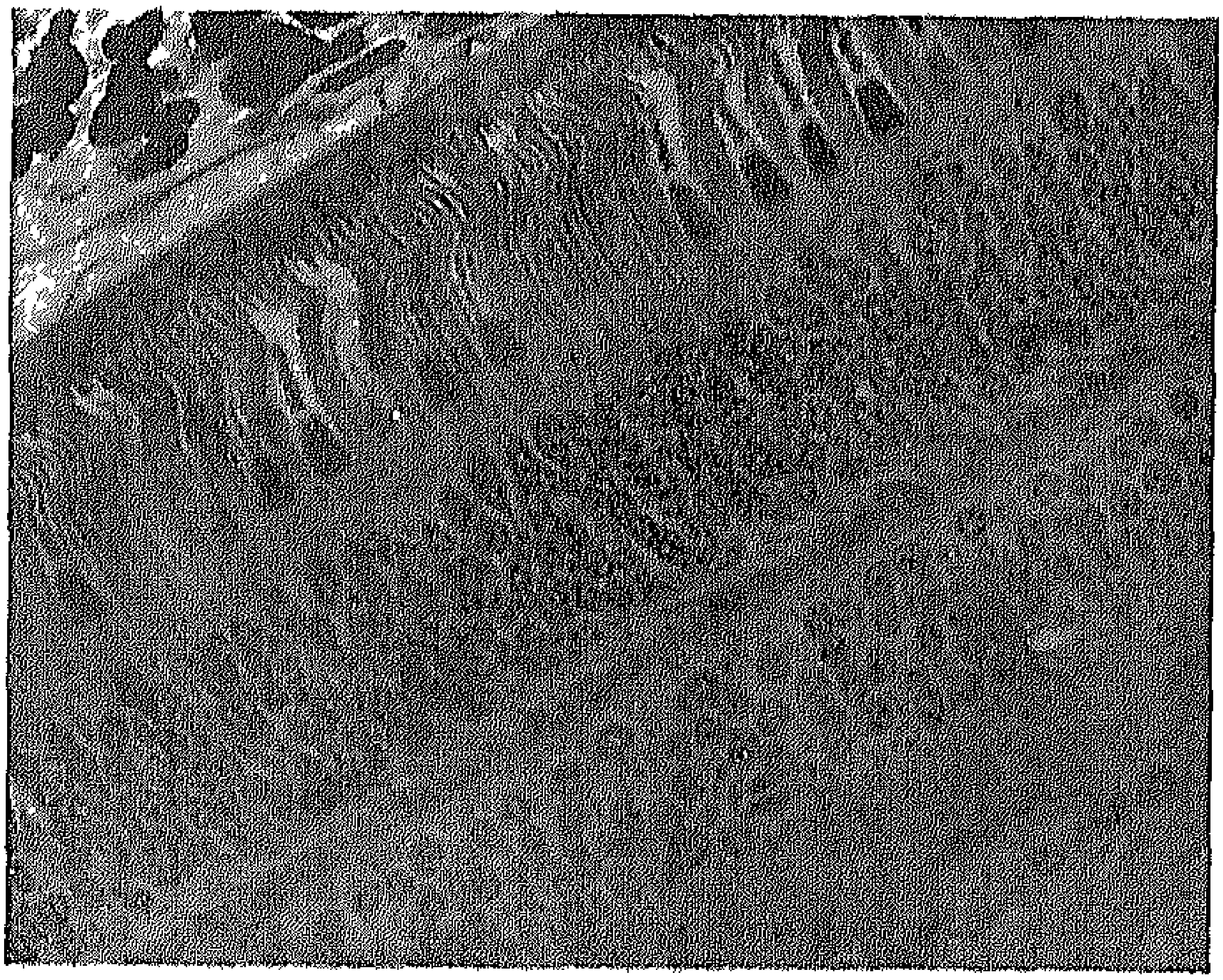


FIG. 259. Section through human retina. Photomicrograph.

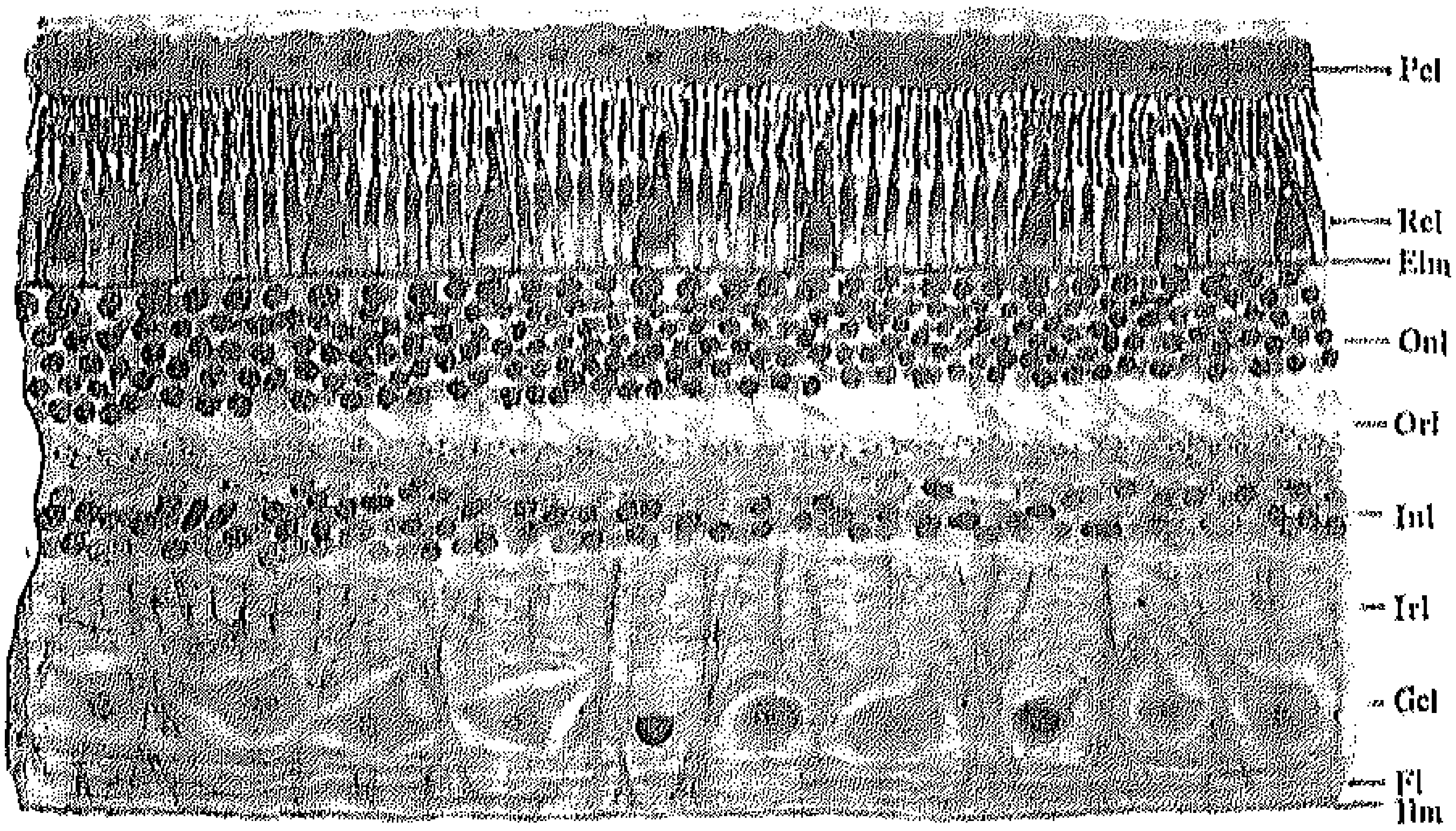


FIG. 260. Section through a human retina. Drawn with the aid of a projectoscope from a preparation by Mrs. M. A. Sharpe (Held's stain). (Pcl) Pigment cell layer. (Rcl) Layer of rods and cones. (Elm) External limiting membrane. (Onl) Outer nuclear (granular) layer. (Orl) Outer reticular (plexiform) layer. (Inl) Inner nuclear layer. (Irl) Inner reticular layer. (Gcl) Layer of ganglion cells. (Fl) Layer of nerve fibers. (Ilm) Internal limiting membrane.

Except at the optic disc and the fovea centralis, the visual portion of the retina consists of the following layers, proceeding inward from the lamina basalis toward the choroid:

1. The layer of pigmented cells
2. The layer of rods and cones
3. The outer limiting membrane
4. The outer nuclear layer
5. The outer reticular layer
6. The inner nuclear layer
7. The inner reticular layer
8. The layer of ganglion cells
9. The layer of nerve fibers
10. The inner limiting membrane

1. THE LAYER OF PIGMENTED CELLS. The layer of pigmented cells consists of a single row of large cells, hexagonal when viewed from the surface, but cuboidal when seen in vertical section. Their nuclei are located in the basal portion of the cell and are surrounded by a layer of clear cytoplasm. The inner portions of these cells are filled with rodlike granules of a dark brown pigment (melanin). Numerous delicate, protoplasmic processes extend from the inner surfaces of the cells between the rods and cones. The pigment migrates from the cells into the processes, and from the processes into the cells, with variations in the

intensity of the light. In strong light the pigment migrates into the processes and forms a protective barrier around the cells. When the light is decreased, the pigment migrates back into the cells.

The outer layer of pigmented cells and the inner nervous or retinal portion represent the *cerebral elements* of the original embryonic optic cup. The space between these elements which is clearly defined in the embryo is still present between the pigmented cells and the layer of rods and cones in the adult. For this reason there is a tendency for the pigmented cells to adhere to the choroid and not to the layer of rods and cones when the two layers are pulled apart.

2. THE LAYER OF RODS AND CONES. The cells of this layer are specialized neuroepithelial elements which react to the stimulus of light that falls on the retina. These cells have certain comparable morphological characteristics but they differ in a few details. They extend through small openings in the external limiting membrane. The outer and inner segments (rod and cone portion) of the cells are located external to the outer limiting membrane, while the portion of the cells containing the nuclei, along with their protoplasmic processes, lie internal to the outer limiting membrane. Each rod and cone cell consists, therefore, of: an outer segment, an inner segment (these make

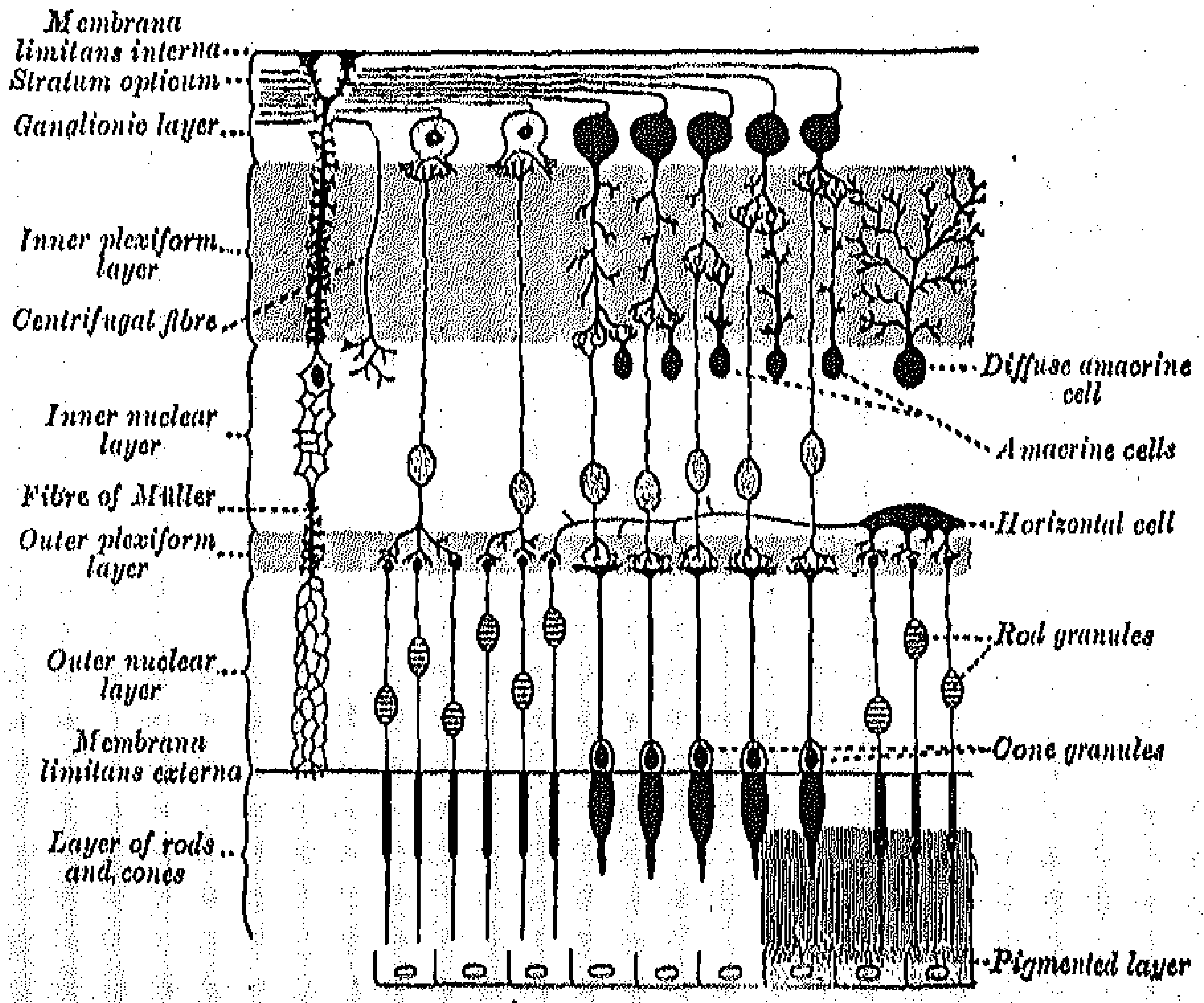


FIG. 261. Plan of the retinal neurones. (From Gray's Anatomy, after Cajal.) (Courtesy, Wolff: "The Anatomy of the Eye and Orbit," Philadelphia, The Blakiston Company.)

up the light sensitive portion of the cell), a nuclear portion, and a process with its termination. The processes of the rod and cone cells end in the outer reticular layer in relation to the dendritic processes of the second order nerve cells. The proportion of rod and cone cells varies considerably throughout the retina. In the macula and fovea only cones are present and they have been estimated to number approximately 17,000 (macula 13,000 and fovea 4,000). In the region close to the macula, rod and cone cells alternate with one another, however, in a very short distance the rods predominate, the ratio being three or four rod cells to one cone cell. This proportion exists throughout most of the retina and continues anteriorly to a point quite near the ora serrata. Krause estimates the total number of rods in the human retina to be 130 million as compared to 7 million cones.

THE RODS. The rods are elongated, cylindrical structures that vary in length from 40 microns (at the ora serrata) to 60 microns in the regions nearer the posterior pole; they are about 2 microns in breadth. They consist of two segments, an *outer* and an *inner segment* which differ both structurally and in staining reaction. The *outer segment* stains black with osmic acid and is possibly closely related to the myelin of nerve fibers. It stains with acid dyes. This segment is longer and more slender than the inner segment, and is doubly refractive to polarized light. The outer segment is enclosed in an external cuticular sheath which is continuous with the sheath of the inner segment. This sheath does not extend over the outer end of the rod. Within the sheath of the outer segment is a homogeneous material which after death appears as a series of disc-shaped fragments which give the outer segment the appearance of being transversely striated. In cross section these discs appear "fluted" and give the outer segment the effect of having fine longitudinally directed parallel furrows. The outer segment contains a substance known as *visual purple (rhodopsin),* which gives the retina its reddish color. In man there is no visual purple in the rods near the ora serrata. On exposure to light the visual purple is destroyed but regenerates rapidly again in the dark.

The *inner segment* of the rod is shorter, thicker and fusiform in shape. It contains a finely granular cytoplasm and takes a basophilic stain. Near its junction with the outer segment it contains a dense appearing ellipsoidal body termed the *fiber apparatus* which shows vertical striations. These striations are produced by numerous highly refractive chromophilic fibers. From the inner end of the rod is given off a fine protoplasmic process, the *rod fiber,* that passes through the external limiting membrane and extends into the outer nuclear layer where it expands into the cell body *(rod granule)* in which the rod nucleus is located. The rod fiber continues into the outer reticular layer where it ends in a knoblike enlargement, the *end bulb.* These end bulbs are in relation to the dendrite processes of the bipolar cells (*rod bipolars*).

THE CONES. In the human the shape of the cones varies, but in general they are conical. They also vary considerably in size. In the fovea centralis they are long and slender (85 microns long and 2.5 microns wide) and gradually become shorter and broader as they progress toward the ora serrata where they are relatively short and wide (22 microns long and 7.5 microns wide).

Like the rods, the cones also have an outer and an inner segment. The *outer segment* is conical in shape. It is enclosed by a sheath which extends over the tip of the segment at one end and is continuous with the sheath of the inner segment at the other. Inside the sheath is a homogeneous, basic staining material that is highly refractive. Vertical grooves are present but are more closely arranged than in the rods.

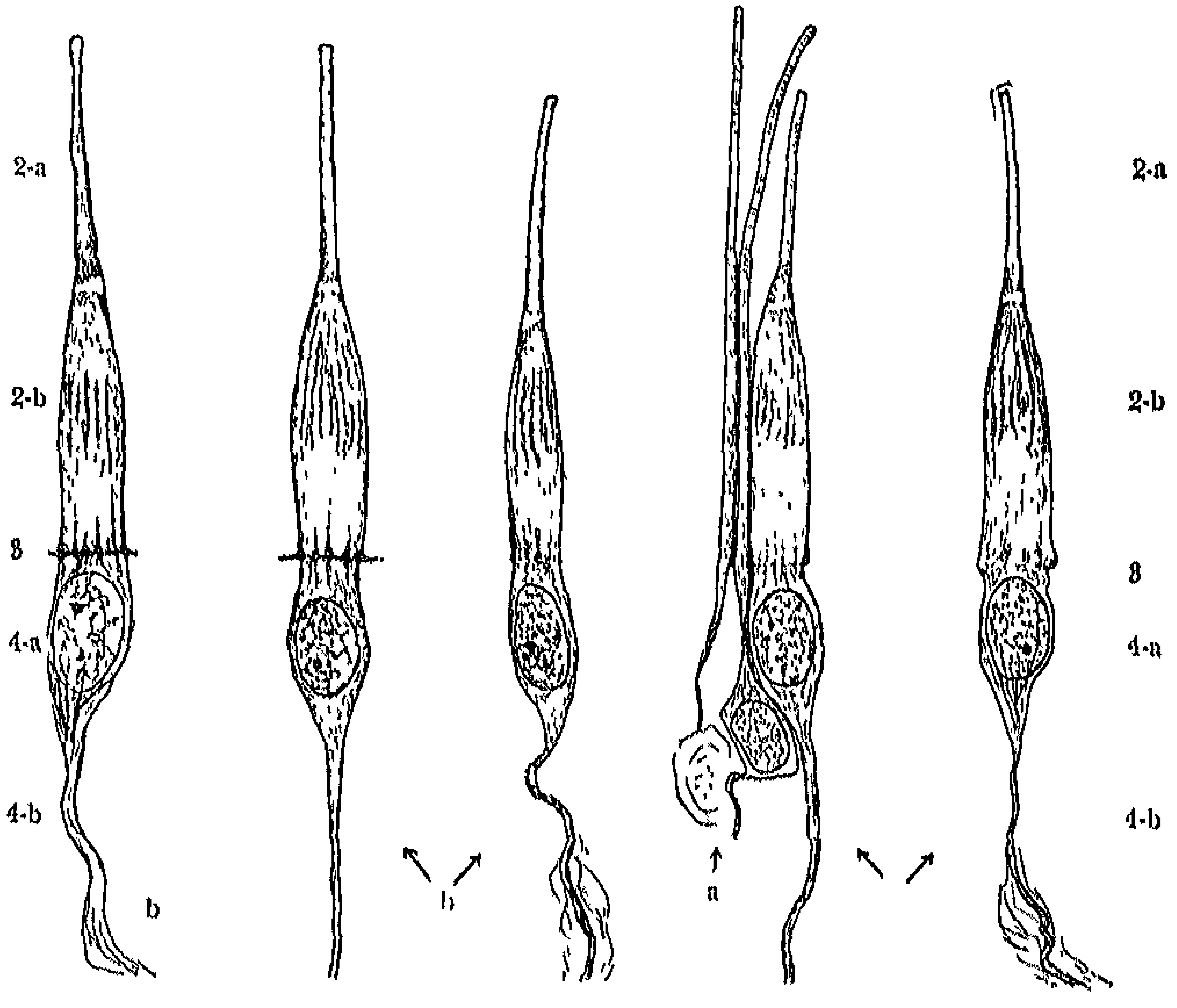


FIG 262. Rods (a) and cones (b) from the retina of an adult Rhesus Macaque. (Preparation of G. W. Bartelmez) Note the long, slender cylindrical shape of the rods as compared with the more conical shape of the cones. The cone nuclei are larger than the rod nuclei and contain distinct round nucleoli. Camera lucida drawing (Courtesy, Polyak: "The Retina," Chicago, The University of Chicago Press)

The *inner segment* is considerably broader than the outer segment and is more or less ellipsoidal in form. It contains an ellipsoid body that is larger than the structure in the rods. The fibers in this structure are not arranged in parallel but rather are interwoven and are extremely fine.

The bodies of the cone cells, which contain the nuclei, are located just internal to the outer *limiting membrane*. The *cone fiber*, which continues the protoplasm of the cone cell, is considerably thicker than the rod fibers. Each cone fiber ends in an expanded *foot plate*, the delicate processes of which are in relation to the end arborizations of the dendrites of the bipolar cells *(cone bipolars)* in the outer reticular layer. The cone cells have to do with the perception of color vision.

3. THE OUTER LIMITING MEMBRANE. The outer limiting membrane is a thin fenestrated membrane *formed of the fibers of Müller*. These fibers, similar to neuroglia, form the main supporting tissue of the retinal coat of the eye.

4. THE OUTER NUCLEAR LAYER. The outer nuclear layer is composed of the nuclei of the rod and cone cells. Only a very small amount of cytoplasm surrounds these nuclei. The rod nuclei are small, spherical bodies that stain densely. They occur at different levels in this layer. *The nuclei of the cone cells are larger, more vesicular, and form a* single row just within the outer limiting membrane. The cone nuclei are separated by definite intervals.

5. THE OUTER RETICULAR LAYER. The outer reticular layer is a narrow area between the outer and inner nuclear layers. It consists of the rod and cone fibers and their endings in relation to the dendritic processes of the bipolar cells. The dendritic process of one rod bipolar cell is related *to the fibers of several rods, but the cone bipolar* anastomoses with the process of only one cone cell.

6. THE INNER NUCLEAR LAYER. The inner nuclear layer contains three principal types of cells: *the horizontal cells* (they form an outer zone of nuclei), the *bipolar cells* (forming the middle zone) and the *amacrine cells* which form the inner zone.

The horizontal cells have elongated and flattened cell bodies with oval nuclei. Their dendrites are in relation to one group of rod and cone cells, while the terminal fibers of their axons are related to another group of rods and cones. Their function is perhaps to coördinate visual impulses between two sets of visual cells.

The bipolar cells are known as the rod bipolar and cone bipolar as they are in relation to the fiber processes of the rod or cone cells. The bipolar cells consist of a slightly oval nucleus surrounded by a small amount of cytoplasm. These cells give rise to two processes: dendritic processes, which extend into the outer reticular layer where they are in relation to the terminal processes of the rod and cone fibers, and axons which extend into the inner reticular layer where they are associated with the dendritic processes of the ganglion cells.

The amacrine cells are peculiar in that they appear to possess richly branched dendrites but no axons. Their dendrites are in relation to processes from the ganglion cells. Some investigators claim to have established the existence of a connection through long, delicate processes by which impulses are transmitted through the amacrine cells from the ganglion cells to the rods and cones.

7. THE INNER RETICULAR LAYER. Like the outer reticular layer, the inner reticular layer is essentially an area occupied by protoplasmic processes from the cells of the adjacent layers. In it the synaptic relations are formed between the axons of the bipolar cells and the dendritic processes of the ganglion cells, as well as the processes of the amacrine cells.

8. THE LAYER OF GANGLION CELLS. The ganglion cell layer is a single row of large multipolar ganglion cells located internal to the inner reticular layer. The ganglion cells contain large vesicular nuclei with deeply staining nucleoli. Nissl bodies and neurofibrillae are present in their cytoplasm. The dendrites of the ganglion cells extend into the inner reticular layer where they come into synaptic relation with the axons of the bipolar cells.

9. THE LAYER OF NERVE FIBERS. The axons of the ganglion cells form the nerve fiber layer on the inner surface of the retina. The fibers are arranged in bundles which converge toward the optic disc where they turn sharply outward, pass through the wall of the eyeball, and are continued to the brain as the optic nerve. Not all fibers of the fiber layer transmit impulses from the retina to the brain *(centripetal fibers)*, some of the fibers pass from cells located in the brain to the retina *(centrifugal fibers)*. These fibers come into relation with the amacrine cells, which are believed to relay their impulses to the rods and cones.

10. THE INNER LIMITING MEMBRANE. The inner extremities of Müller's fibers form expansions which, when joined together, constitute the inner limiting membrane lying between the fiber layer and the hyaloid membrane.

As mentioned previously, Müller's fibers form the main supporting elements of the retina. These fibers give off lateral processes which break up into fine branches. These branches form a reticulum which gives support to the nervous elements of the retina. In the region of the inner nuclear layer, Müller's fibers expand and form small masses of protoplasm which enclose oval nuclei. The outer ends of the fibers also form expansions, the expansions uniting and constituting the outer limiting membrane. Numerous delicate fibers extend from the outer limiting membrane between the rods and cones which they support. Other supporting elements are neuroglia cells of the astrocyte type, which occur in the ganglion cell layer and in the layer of nerve cells.

THE MACULA LUTEA. The macula lutea is a thickened area, oval in outline, which lies lateral to the posterior pole. The thickness of the macula is due to an increase in the number of cells in the ganglion cell layer, the increase being from a single row of cells outside of the macula to a layer in which eight or more rows of cells may be present. A similar increase takes place in the inner nuclear layer.

THE FOVEA CENTRALIS. The fovea centralis is a small depression in the middle of the macula lutea, in which the thickness of the retina is greatly reduced to give the least interference with the passage of light. Cones are the only visual elements present in the fovea. The reticular layers are combined in a single layer immediately beneath the fovea, in which only a few bipolar cells are present. The ganglion cell layer is entirely absent in the fovea, the cells being displaced outward into the outer area.

Owing to the fact that the nuclear layers are located to one side of the depression, the cone fibers are directed obliquely and are considerably lengthened, constituting a special arrangement known as the *fiber layer of Henle*. The choroid is also thickened opposite the fovea, the increase taking place in the choriocapillaris. The yellow color of the macula is not due to the presence of a special pigment, but to the manner in which light is reflected from the inner retinal layers.

The visual elements disappear close to the border of the ciliary body, at which point the thickness of the retina is abruptly diminished. The rods are the first to be lost and they are soon followed by the cones which become rudimentary before they disappear. This transition takes place along an irregular line known as the ora serrata. Anterior to the ora serrata, Müller's fibers are replaced by the unpigmented columnar cells of the pars ciliaris. These cells gradually diminish in size and at the junction of the ciliary body with the iris acquire pigment granules, both layers of the retina being pigmented on the posterior surface of the iris.

The blood supply of the retina is through the central retinal artery. This artery enters in the optic nerve and emerges on the nasal side of the optic disc where it breaks up into branches. The larger branches continue in the fiber layer where they give off smaller branches which end in capillary networks in the inner reticular and nuclear layers. The outer nuclear layer and the layer of rods and cones which are avascular receive their nutritive material from the choriocapillaris of the choroid. In general, the veins follow the course of the arteries.

The lymphatics form perivascular spaces about the blood vessels,

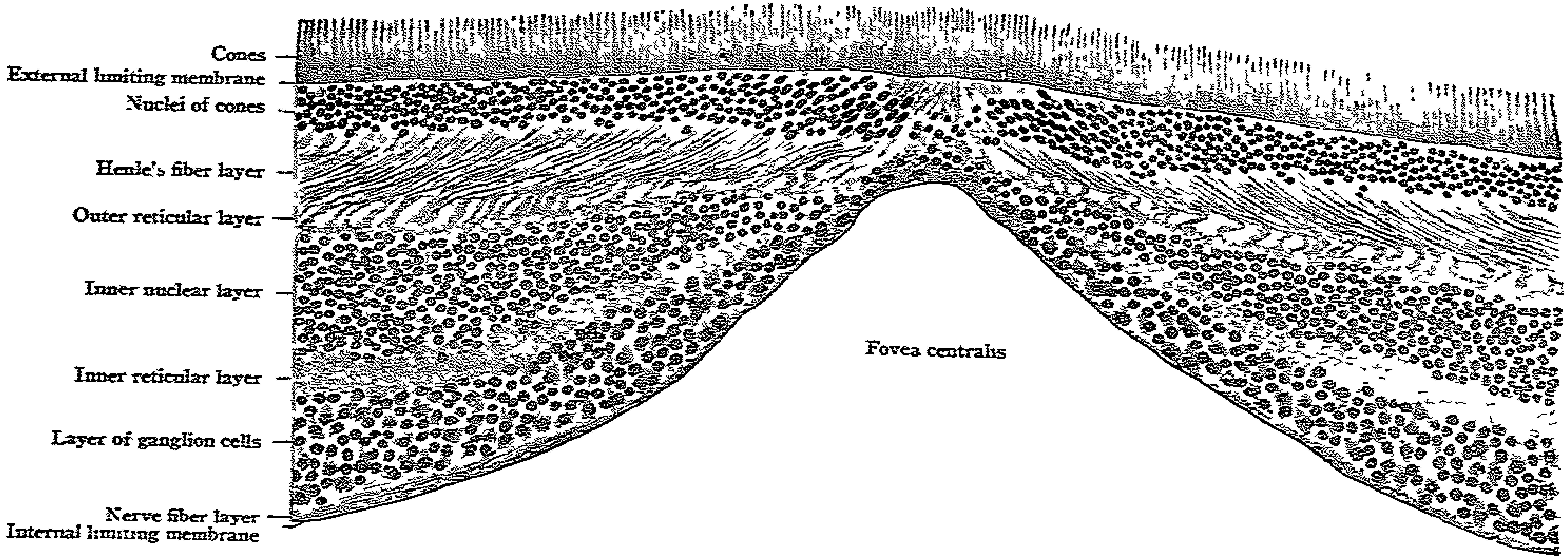


FIG. 263. Horizontal section through the macula and the fovea of a man sixty years old 135 ×. (Schäfer.) The nerve fiber layer like all layers, is thicker on the side toward the papilla of the optic nerve than on the opposite side. In the latter situation the nerve fibers are seen in transverse section as minute dots. The section is not through the exact center of the fovea, for there only cone cells are present. No remnants of the confluence of the inner granule and ganglion cell layers are found. (Courtesy, Bremer-Weatherford: "Text-book of Histology," Philadelphia. The Blakiston Company.)

THE ANTERIOR DIVISION OF THE EYE

The anterior division of the eye begins at the general plane of the *ora serrata and includes:* 1. *the cornea,* 2. *the ciliary body,* 3. *the iris,* and 4. the *lens.*

1. THE CORNEA. The cornea constitutes the anterior one-fifth of the eyeball. It is a continuation of the sclera, but differs from it in its greater curvature and the transparency of its substance. It is an important part of the refracting mechanism of the eye, its refractive power being nearly twice that of the lens. The zone in which the transparent substance of the cornea merges into the sclera is known as the *limbus,*

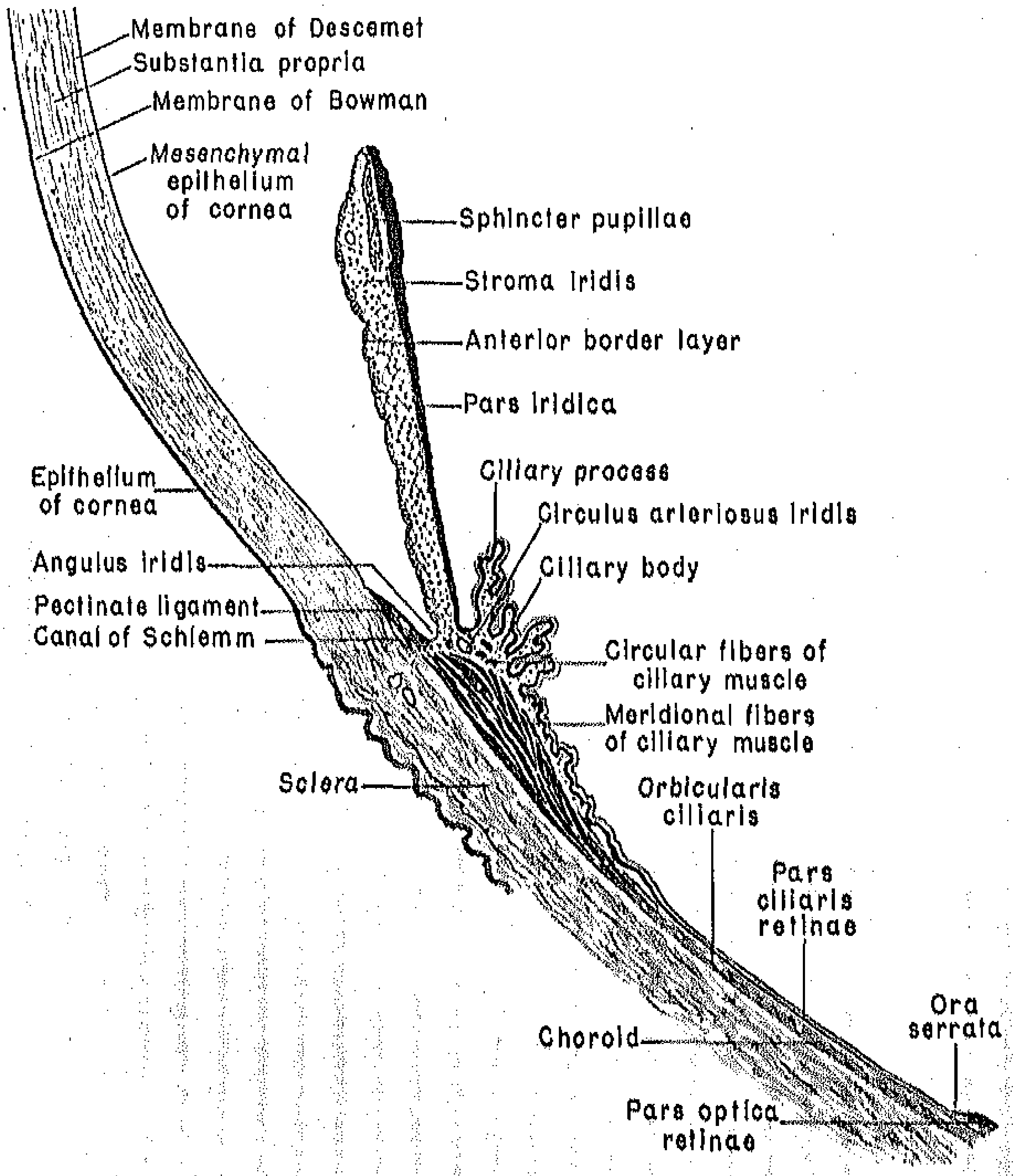


FIG. 264. Meridional section through the anterior part of the eye.

the position of which is marked by a slight groove encircling the border of the cornea. Beginning at the outer surface, the cornea consists of the following layers:

The epithelial layer
The anterior basal membrane (membrane of Bowman)
The substantia propria
The posterior basal membrane (membrane of Descemet)
The mesenchymal epithelial layer (usually referred to as the endothelial layer)

THE EPITHELIAL LAYER. The epithelial layer forms the external covering of the cornea. It is a thin, stratified squamous layer which is continuous with the conjunctival epithelium of the sclera. It consists of several rows of distinctly outlined cells, the basal layer of which is composed of cuboidal or low columnar cells with characteristically rounded outer ends. The nuclei are slightly oval. The basal surfaces of these cells are provided with toothlike projections by which they are more firmly attached to the basal membrane. The cells of the intermediate layers are polyhedral with round or oval nuclei and more deeply staining cytoplasm than the cells of the basal layer. The cells of the outer layer are flat, with flattened oval nuclei. Under normal conditions the cells of the outer layer do not become keratinized.

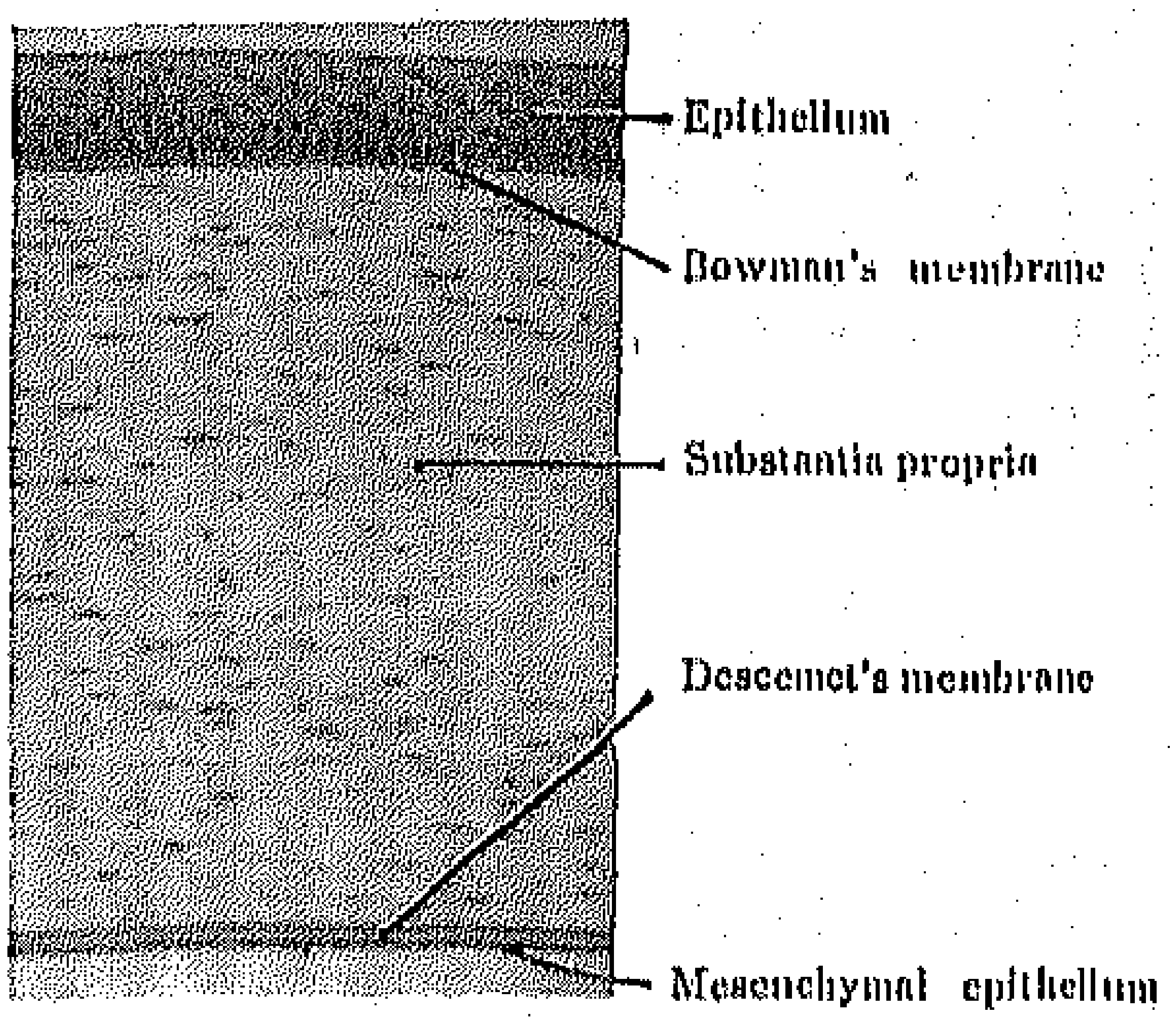


FIG. 265. Section through human cornea. Photomicrograph.

THE ANTERIOR BASAL MEMBRANE (BOWMAN'S MEMBRANE). This layer is the thick homogeneous membrane on which the epithelial layer rests. Formerly this layer was known as the "outer elastic membrane." However, it does not possess elastic properties, but serves as a protective layer on the outer surface of the substantia propria, of which it is believed to be a modified portion. Although homogeneous in appearance, its fibrous character can be demonstrated by appropriate methods.

THE SUBSTANTIA PROPRIA. This layer forms the principal part of the cornea. It is directly continuous with the sclera and like the sclera, consists of collagenous fibers arranged in flattened bundles, the bundles lying parallel to one another in the same plane, but crossing those of alternating planes at right angles. The fibers and fiber bundles are bound together by an intercellular cement, a substance which probably is more or less fluid in its nature. The cellular elements, known as the corneal corpuscles, are located in the spaces between the fiber bundles with the processes of the cells, in the same level, anastomosing with one another. Lymphocytes and granular leucocytes are present in the interfibrillar spaces, their number increasing whenever the cornea becomes inflamed. Fibers known as *arcuate fibers* pass between the lamellae and serve to bind them together. Elastic fibers are present but they are more numerous in the region of Descemet's membrane than elsewhere in the cornea.

THE POSTERIOR BASAL MEMBRANE (DESCEMET'S MEMBRANE). This is a thin, homogeneous layer between the substantia propria and the mesenchymal epithelial layer and is regarded as forming the basement membrane on which the mesenchymal epithelial layer rests. Its elastic properties are indicated by its reaction to selective stains.

The outer portion of the sclera overlaps the margin of the cornea. This condition is reversed, however, on its inner margin where Descemet's membrane breaks up into fine fibrous bundles at the sclerocorneal

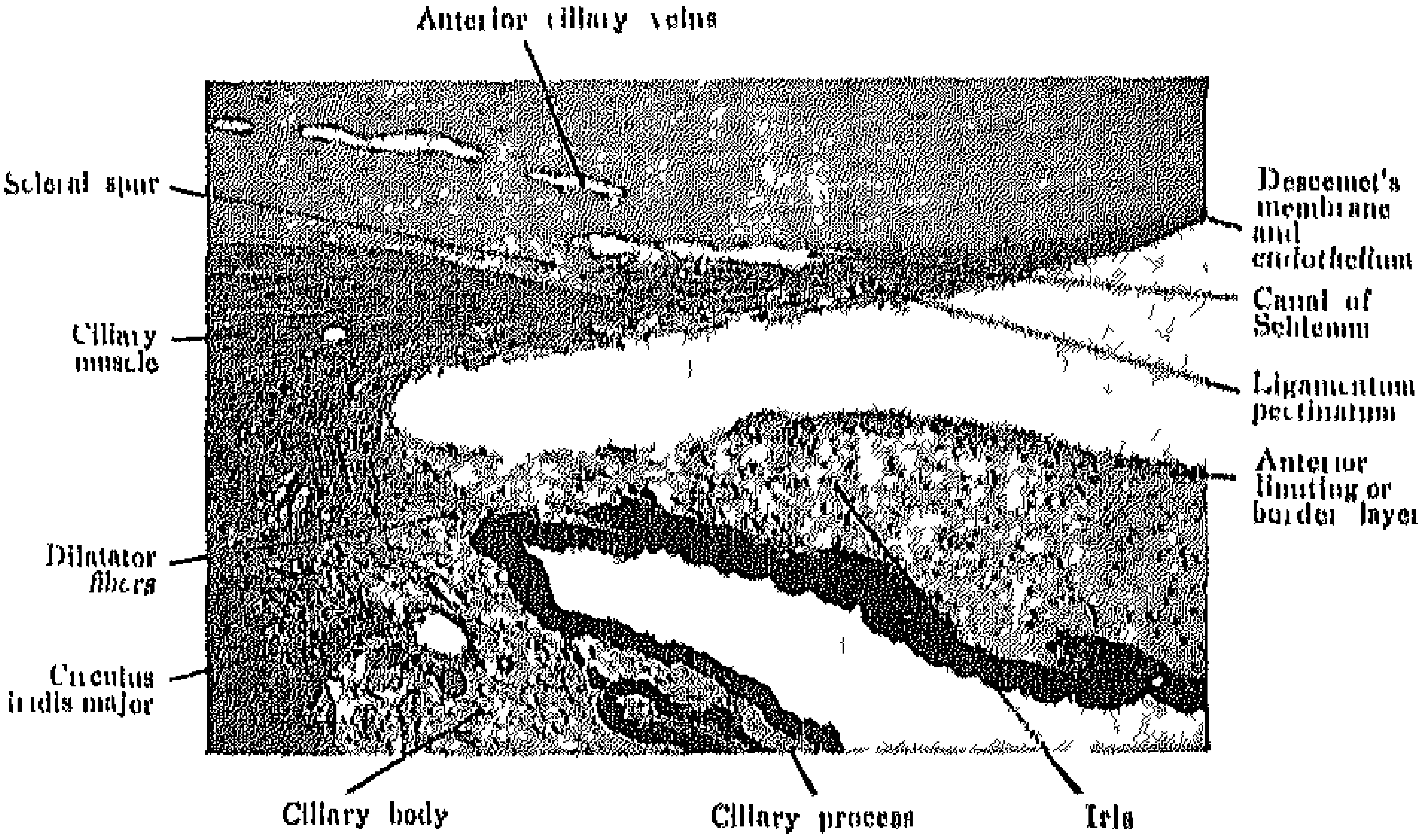


FIG. 266. Section of the angle of the anterior chamber. (Courtesy, Wolff: "The Anatomy of the Eye and Orbit," Philadelphia, The Blakiston Company.)

junction. Some of these fibers provide for the attachment of the ciliary muscles, others form the inner boundary of a venous canal, the *canal of Schlemm (sinus circularis iridis)* which encircles the eyeball close to the margin of the cornea. The fibers which extend from Descemet's membrane and form the lateral wall of the anterior chamber of the eye, continue around the iridial angle to the root of the iris and constitute the *pectinate ligament (ligamentum pectinatum iridis).* The fibers of the pectinate ligament enclose a number of spaces, the *spaces of Fontana,* through which fluid may pass from the anterior chamber of the eye into the canal of Schlemm.

THE MESENCHYMAL EPITHELIAL LAYER (POPULARLY TERMED ENDOTHELIAL LAYER). This layer consists of a single layer of flattened cells which lines the inner surface of the cornea and is continued about the fibers of the pectinate ligament, thus providing an epithelial lining for the spaces of Fontana. Continuing over the iridial angle it extends upon the anterior surface of the iris.

The cornea itself is avascular. It receives nutritive material from a number of capillaries which form a network about its margin in the region of the limbus.

Branches from the ophthalmic nerves enter the substantia propria from the networks about the corneal border. These fibers pass between the lamellae and after perforating Bowman's membrane, they end between the cells of the epithelial layer.

2. THE CILIARY BODY. The ciliary body is that part of the choroid which lies between the ora serrata and the sclerocorneal junction. It forms a thickened muscular ring encircling the eyeball, which appears triangular in form when seen in section. Its outer surface is adjacent to the sclera while its inner surface is covered by the anterior extension of the nonvisual portion of the retina *(pars ciliaris).* On its inner surface there are a number of folds which project inward and are known as the *ciliary processes.*

The first part of the ciliary body, the *orbicularis ciliaris,* consists of a firm, fibrous, deeply pigmented structure containing the veins which convey blood from the ciliary body and the iris. It forms a smooth ring about the inner surface of the eyeball just anterior to the ora serrata.

The second part consists of the smooth muscle fibers of the *ciliary muscle.* These fibers are arranged in an outer, *meridional layer,* a middle, *radial layer* and an inner, *circular layer.* The meridional fibers (muscle of Brücke) arise from an extension of the sclera near the canal of Schlemm and extend backward to be inserted into the anterior border of the orbicularis. The radial fibers originate with the meridional fibers but curve inward toward the ciliary processes, into the roots of which they are inserted. The bundles into which the radial fibers are gathered, are separated by bands of connective tissue in which numer-

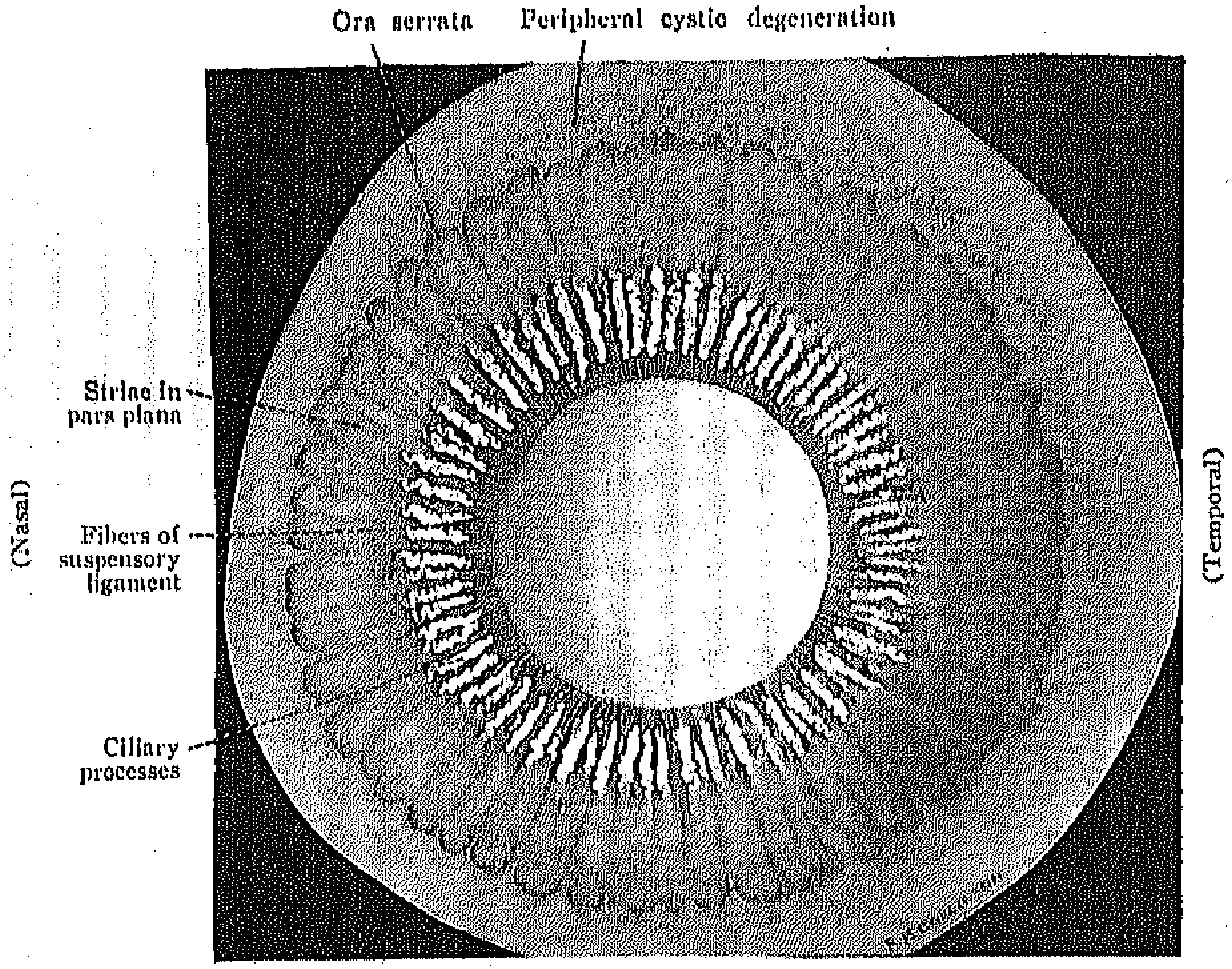


FIG. 267. Ciliary body, suspensory ligament, lens and ora serrata seen from behind. Note that the teeth of the ora serrata are the worst marked on the temporal side where cystic degeneration (shown by mottled appearance) is best developed. (Courtesy, Wolff: "The Anatomy of the Eye and Orbit," Philadelphia, The Blakiston Company.)

ous elastic elements are present. The circular fibers (ciliary muscle of Müller) form a ring about the eyeball at the inner angle of the ciliary muscle close to the root of the iris.

The contraction of the fibers of the ciliary muscle lessens the pull of the suspensory ligament on the elastic lens capsule, the lens becoming by its own elasticity more convex. The focal distance of the rays of light passing through the refractive media of the eye, are altered by the changes which take place in this manner in the curvature of the lens.

The *ciliary processes* consist of 70 to 80 meridionally directed ridges on the inner surface of the ciliary body. These ridges are low at the orbicularis but increase to the height of a millimeter or more opposite the equatorial region of the lens. They consist of a delicate stroma of connective tissue, continuing the connective tissue stroma of the ciliary body, in which numerous elastic fibers are present. The stroma of the ciliary processes is covered by the nonvisual portion of the retina which forms the pars ciliaris.

The principal blood supply of the ciliary body is by arteries which form a circle about the eyeball at the root of the iris *(circulus arteriosus*

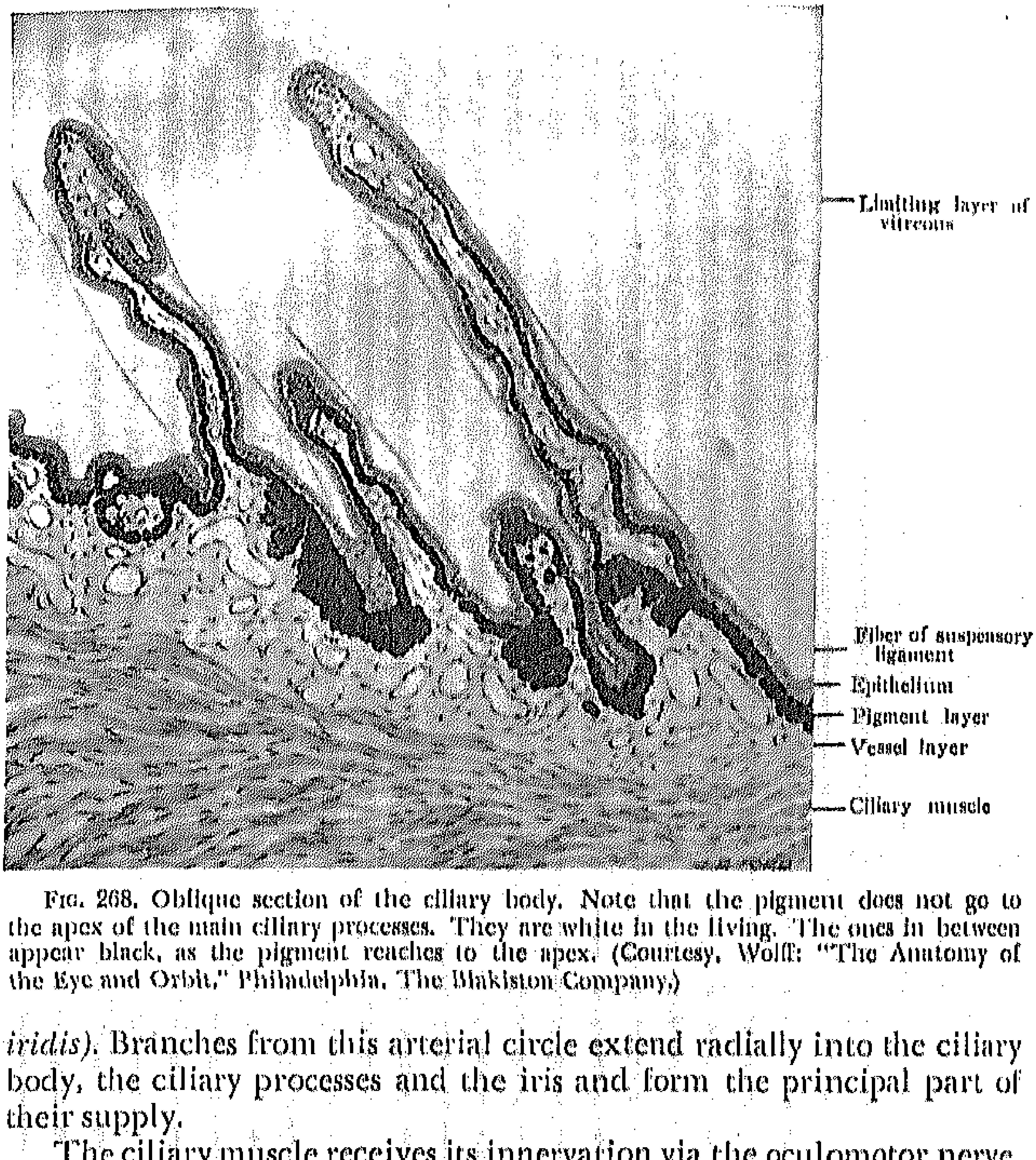


FIG. 268. Oblique section of the ciliary body. Note that the pigment does not go to the apex of the main ciliary processes. They are white in the living. The ones in between appear black, as the pigment reaches to the apex. (Courtesy, Wolff: "The Anatomy of the Eye and Orbit," Philadelphia, The Blakiston Company.)

iridis). Branches from this arterial circle extend radially into the ciliary body, the ciliary processes and the iris and form the principal part of their supply.

The ciliary muscle receives its innervation via the oculomotor nerve, ciliary ganglion and short ciliary nerves. The nerves to the ciliary muscle are the fibers of the oculomotor nerve. The postganglionic fibers from the ciliary ganglion reach the ciliary muscle by way of the short ciliary nerves. Sensory fibers are also said to be present.

3. THE IRIS. The iris is a circular, curtainlike fold extending inward from the ciliary body, in front of the lens. It bounds a more or less central, circular opening, the *pupil*. The portion of the iris which bounds the pupil is known as the *pupillary border*. The root of the iris is attached to the ciliary body from which connective tissue fibers pass into its posterior part. Fibers from the pectinate ligament pass into its anterior part. These fibers are arranged in bundles, between which are interfibrillar clefts or lymph spaces. A thin layer of mesenchymal epi-

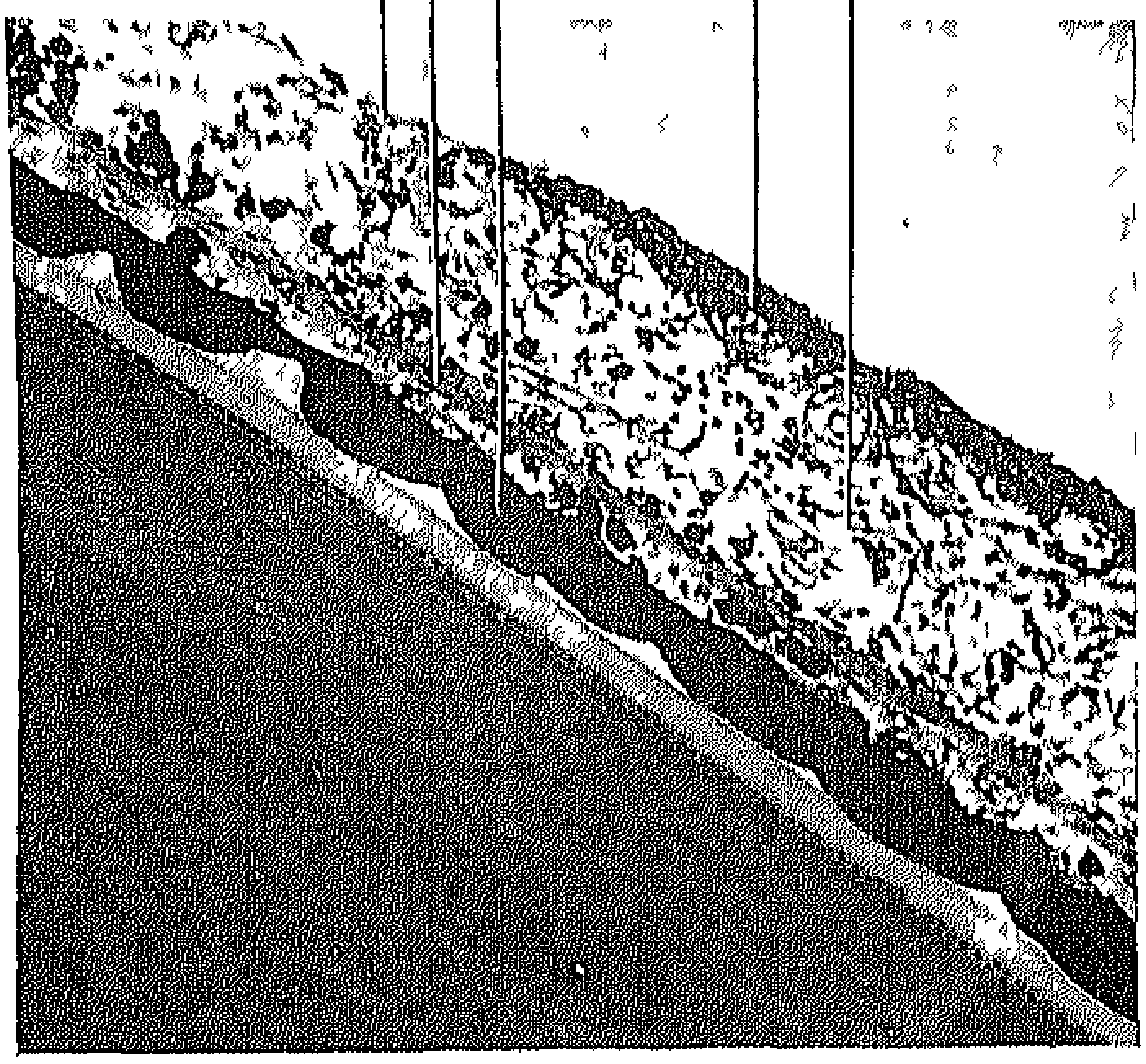


FIG. 269 Vertical section of a portion of the human iris and lens. The iris is applied so closely to the lens that the posterior chamber of the eye is practically obliterated. Photomicrograph.

thelial cells rests upon, but does not form a complete covering over, the entire anterior surface of the iris. Open spaces appear here and there in the mesenchymal epithelial layer, through which the lymph spaces of the stroma communicate with the anterior chamber of the eye. These spaces also communicate with the spaces of Fontana. The inner, or posterior surface of the iris is covered by a two-layered extension of the retina which is known as the *pars iridica*.

In the tissue immediately beneath the mesenchymal epithelial layer (called endothelium in most texts) the large, branched stellate cells are quite close together and may be several layers in depth. They are supported by a relatively small number of connective tissue fibers among which no blood vessels are present. This portion of the stroma is known as the *anterior border layer*. The cells of the anterior border layer are heavily pigmented in dark-eyed persons, but only lightly so in those who have blue eyes. The blue color is due to the reflection of light through this layer, from the more heavily pigmented cells in the posterior layers.

The portion of the retina which lies on the posterior surface of the

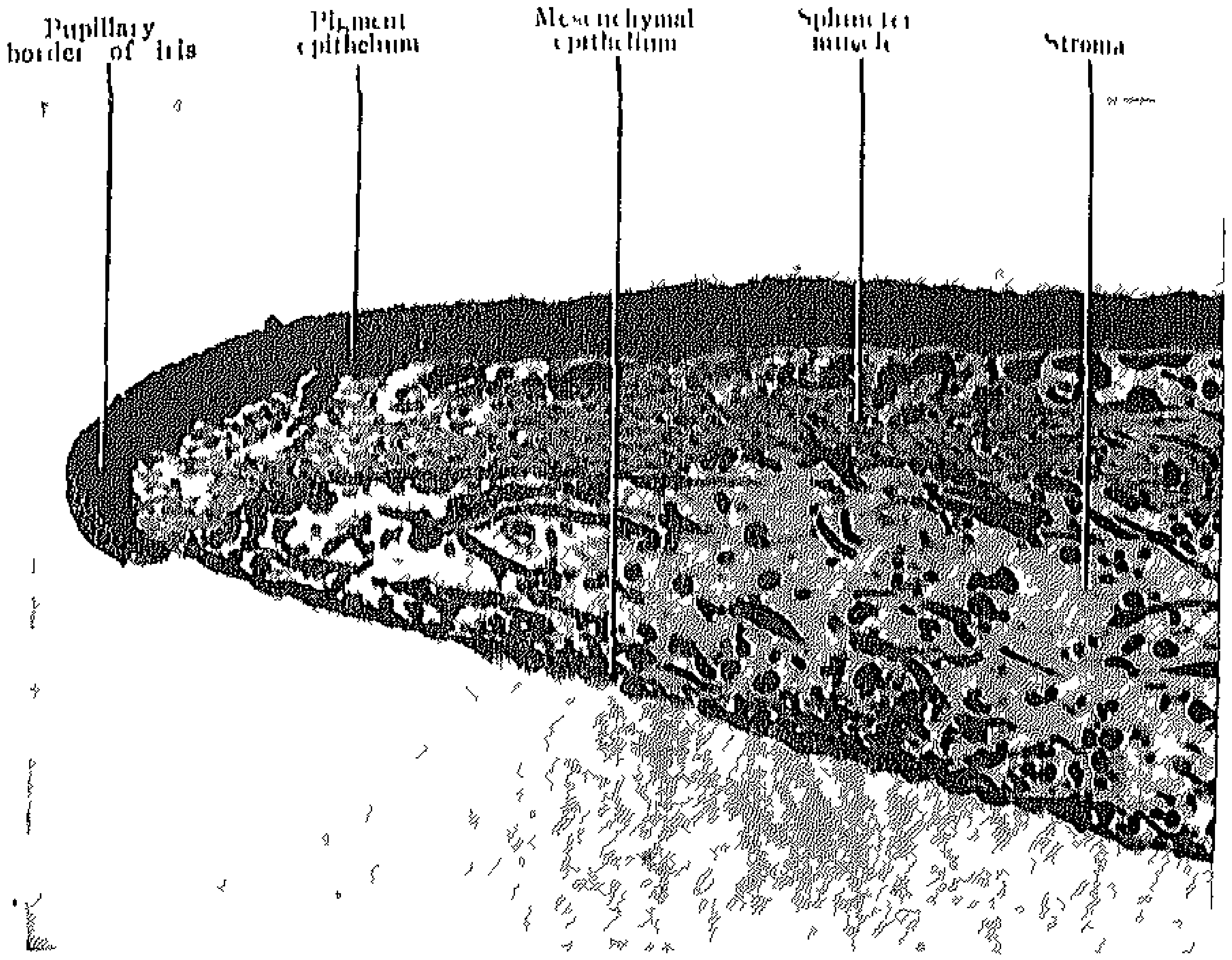


FIG. 270 Vertical section of the pupillary portion of a human iris. About one fifth of the entire width of the iris is shown. Photomicrograph.

iris consists of two rows of cells both of which are heavily pigmented. This layer ends abruptly on the pupillary border.

Between the pigmented epithelium and the anterior border layer, the connective tissue fibers give support to numerous thick-walled blood vessels, which form a vascular layer. These vessels are branches of the circulus arteriosus, from which they extend radially toward the pupillary border. A peculiarity of the vessels of the iris is that their walls are formed by connective tissue fibers only and contain no muscular or elastic fibers, although elastic fibers are plentifully present in the supporting stroma. Numerous branched, pigmented cells are intermingled with the connective tissue fibers in the vascular layer.

Two sets of contractile elements are present in the iris: the *sphincter pupillae muscle* and the *dilator pupillae muscle*. The sphincter is a thick ring of smooth muscle fibers located in the vascular layer just within the pupillary border. The dilator muscle consists of a layer of fiberlike cells, extending from the pupillary border to the root of the iris. These cells are located between the pigmented epithelium and the vascular layer. The dilator muscle consists of a contractile portion which is toward the vascular layer, and a nucleated portion which has the appearance of being a part of the pigmented layer. The morphology of the elements which form the dilator muscle has been the subject of some debate. It is now generally believed that they are derived from the epithelial cells of the retinal layer and therefore, are myoepithelial structures.

The muscular tissues of the iris are supplied by branches from the ciliary nerves. The sphincter is innervated by postganglionic fibers from the ciliary ganglion. The preganglionic fibers originate in the autonomic portion of the oculomotor nucleus and reach the ganglion over the oculomotor nerves. The dilator pupillae is innervated by postganglionic fibers of the thoracolumbar system, originating in the superior cervical ganglion and reaching the eye via the carotid plexus and short ciliary nerves.

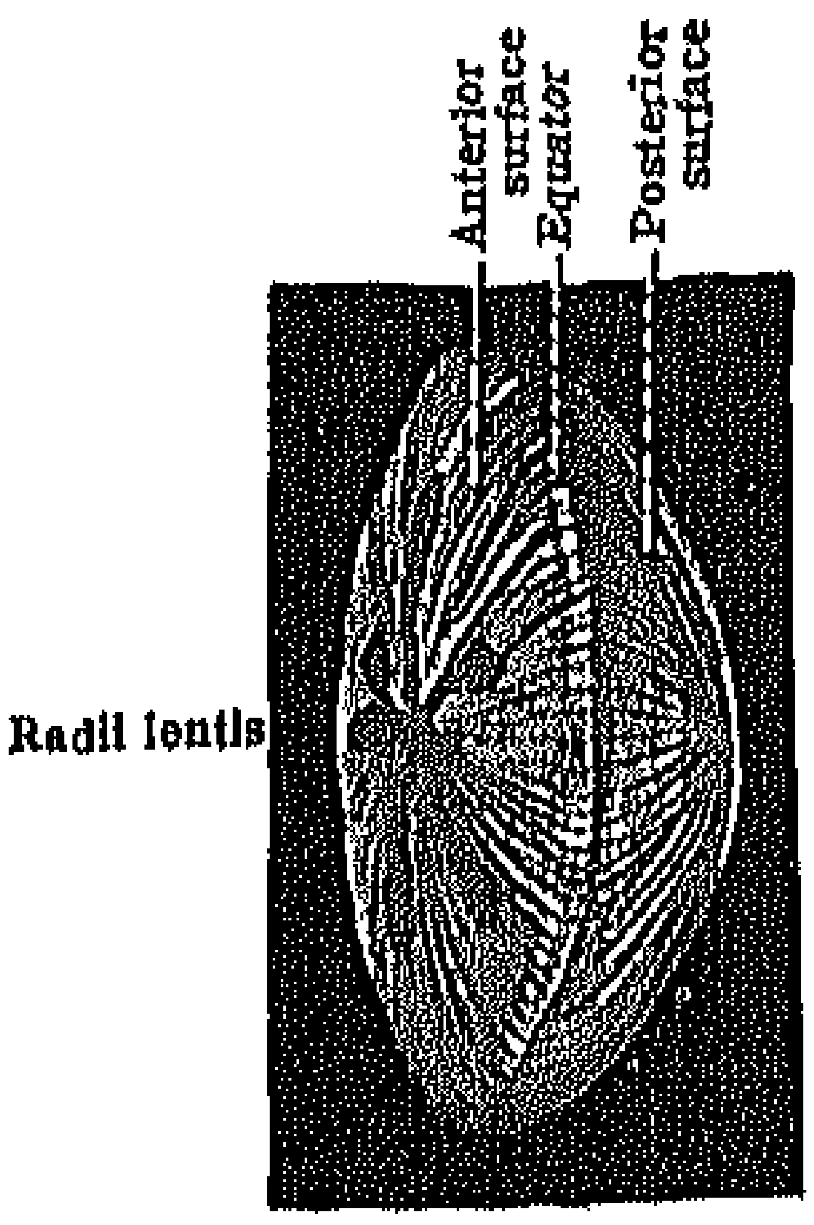


FIG. 271. Lens viewed from side. 4 ×. (Courtesy, J. Parsons Schaeffer, Ed.: "Morris' Human Anatomy," Philadelphia, The Blakiston Company.)

4. THE LENS. The lens is a transparent, biconvex body located immediately behind the iris. Its posterior curvature being somewhat greater than its anterior curvature and its posterior surface rests in a depression on the anterior part of the vitreous body. The distance between the mid-point of the anterior surface of the lens to the mid-point of its posterior surface is about 4 mm., its vertical diameter in the equatorial plane varies from 8-10 mm. The lens is enclosed by a transparent, elastic membrane, the *lens capsule*. It is attached to the ciliary body by the *suspensory ligament*.

The lens epithelium is a single layer of cuboidal cells covering its anterior surface, immediately beneath the anterior portion of the capsule. These cells which are elongated toward the equator are transformed into flattened, six-sided prisms, the *lens fibers*, which are held together by an interfibrillar cement. The nuclei lie in the superficial part of the lens, in the region where the transformation of the cells into lens fibers takes place. This region is known as the *nuclear* or *transitional zone*.

In the growth of the lens, the fibers which are formed first are overlaid by those which are formed later. This results in the fibers being arranged in concentric layers or lamellae. The more deeply placed lamellae degenerate and harden, forming the lens nucleus. The superficial lamellae are softer and can be compressed when the ciliary muscles pull on the substance of the lens. By the relaxation of the tension on the lens capsule and by the elasticity of the lens, its curvature is altered and its focal adjustment changed.

5. THE SUSPENSORY LIGAMENT. The suspensory ligament consists of fibers by which the lens is attached to the ciliary body. These

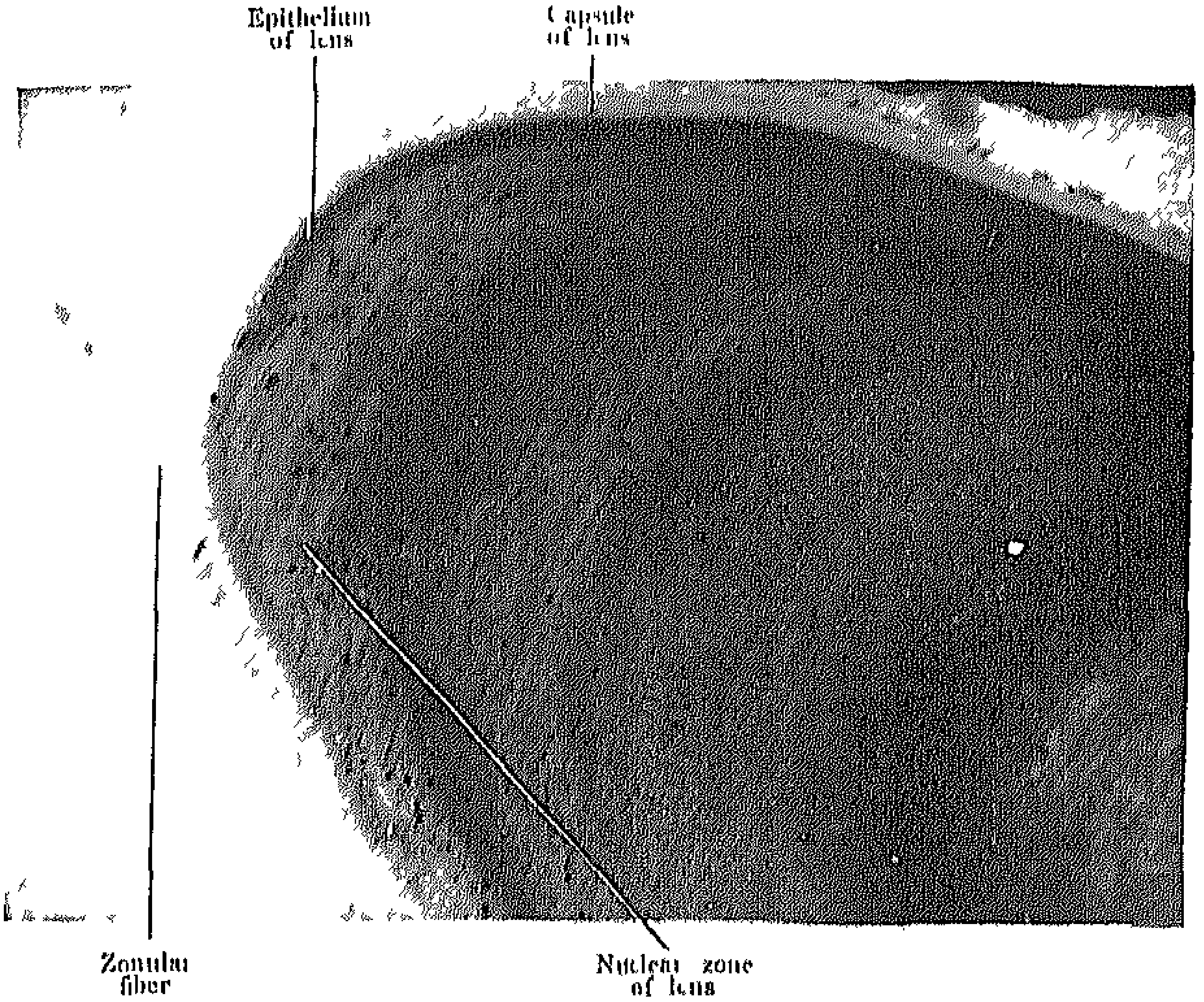


FIG. 272 Meridional section through the marginal portion of a lens. Photomicrograph.

fibers, which are derived from the orbicularis ciliaris and the corona ciliaris, pass radially over and between the ciliary processes, to insert into the lens capsule in two bands, one in front and one behind the lens equator. The triangular space which is formed between the diverging fibers was once thought to be a specialized channel, the *canal of Petit.* The entire zone occupied by the fibers of the suspensory ligament as they encircle the lens, is known as the *zonule of Zinn.*

THE OPTIC NERVE

The optic nerve is composed of fibers which extend from the retina to the brain. As has already been pointed out, these fibers are the axons of the ganglion cells in the layer of that name in the retina. Within the eyeball the fibers are gathered into bundles which converge on the optic disc, where they turn outward and pass through the *lamina cribrosa* of the sclera. After passing through the lamina cribrosa the fibers acquire a myelin sheath but are not enveloped by a neurilemma.

The optic disc is a nonvisual area about 1.5 mm. in diameter and is known as the "blind spot" of the retina. The retinal fibers are arched as they turn to enter the disc. This results in the formation of a depres-

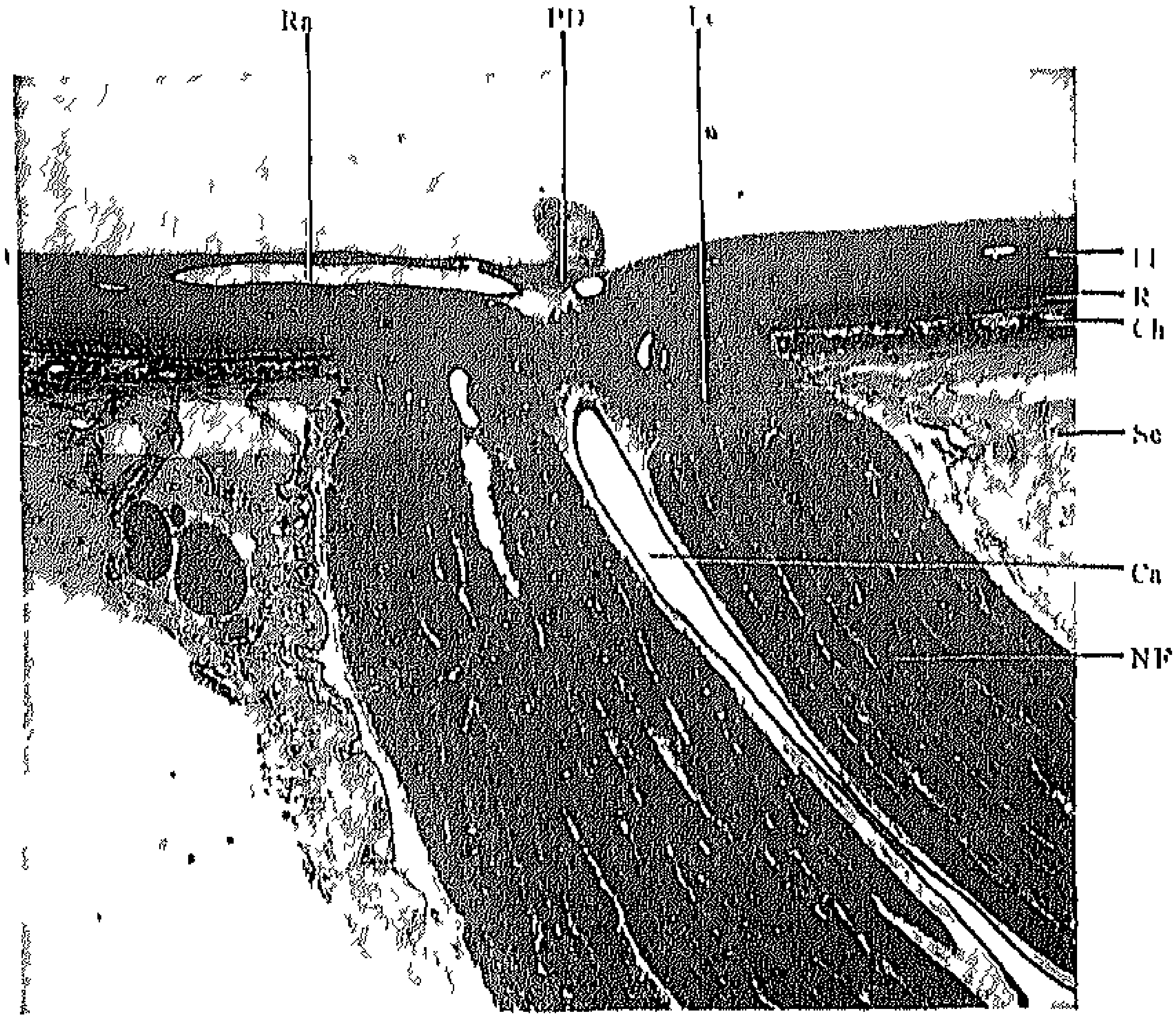


FIG. 273. Posterior segment of the eye, showing the emergence of the optic nerve. (Ca) Central artery. (Ch) Choroid. (Fl) Fiber layer. (Lc) Lamina cribrosa. (NF) Fibers of the optic nerve. (PD) Physiological depression (blind spot). (R) Retina. (Ra) Retinal artery. (Sc) Sclera. Photomicrograph

sion in the middle of the disc which is known as the *physiological depression.*

The fibers of the optic nerve are arranged in bundles, the bundles being surrounded by septa of connective tissue. Neuroglia elements are to be found among the nerve fibers. The axial portion of the nerve is occupied by the retinal artery and vein which enter it a short distance behind the eyeball. Branches of the artery extend through the connective tissue septa and supply the various parts of the nerve.

Since the optic nerve is an outgrowth of the brain, it is enclosed by extensions of the membranes by which the brain is invested. These are: the outer or *dural sheath,* the fibers of which intermingle in the eyeball with the fibers of the outer third of the sclera. A thin membrane, continuing the *pia mater,* is closely applied to the nerve and sends fibrous extensions in the form of septa, between the bundles of nerve fibers. The fibers of the *pial sheath* become continuous with those of the inner third of the sclera.

The space between the dural and pial sheaths is called the *intervaginal space.* A thin membrane representing the *arachnoid,* divides this space into two parts: the *subdural space* between the arachnoid and the dura, and the *subarachnoid space* between the arachnoid and the pia. These spaces are crossed by delicate fibers which connect the arachnoid with the dura and also with the pia. The fibers connecting the arachnoid with the pia are more numerous than those connecting it with the dura. The subarachnoid space of the optic nerve is continuous with that of the brain and contains cerebrospinal fluid. Increased pressure of the latter is reflected, therefore, by pressure upon the optic nerve fibers and the retinal artery and vein, leading to papilledema and diminished vision. These are important diagnostic signs of intracranial disease.

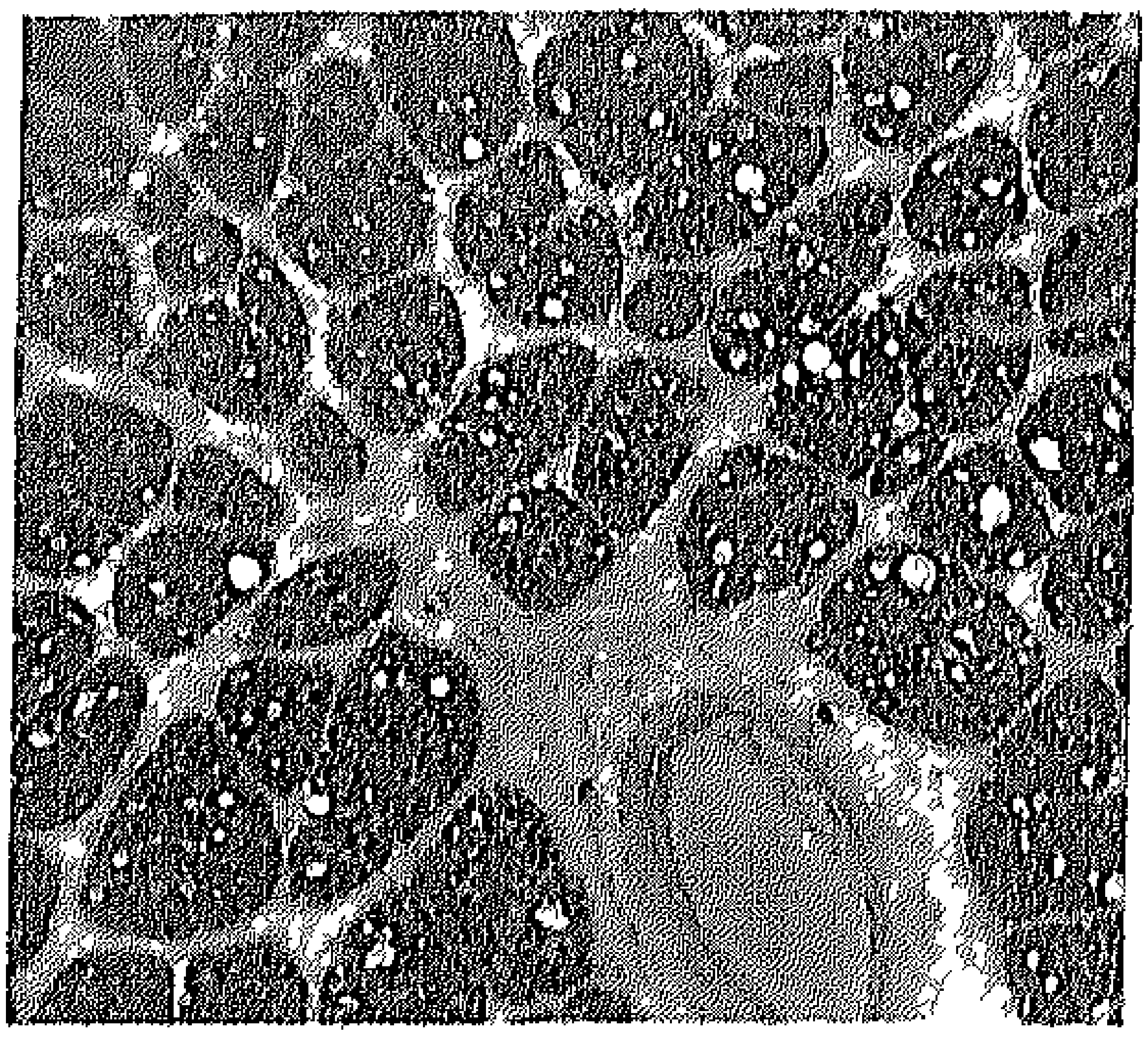


FIG. 271. Partial section through optic nerve showing central retinal artery. Photomicrograph

THE EYELID

The eyelids *(palpebrae)* are two folds of skin, one above (upper eyelid) and one below (lower eyelid) and so arranged that they can be drawn over the front of the eye for its protection. Their involuntary movement not only keeps the lacrimal fluid (tears) spread over the exposed portion of the eyeball, thus preventing the drying of the tissue, but it also serves for the removal of particles of dust which have settled on the anterior or exposed portion of the eyeball.

The outer surface of each fold is covered with a thin layer of integument, beneath which the subcutaneous tissue consists of loosely arranged collagenous and elastic fibers. Small, delicate hairs are scattered over this surface, associated with which are both sebaceous and sweat glands.

The integument is continued over the anterior angle of the lid and forms the covering of the free or *palpebral* border. This bears two or three rows of coarse hairs, the *eyelashes* or *cilia*. The cilia are set in follicles that are directed obliquely and extend deeply into the subepithelial tissue. Modified sebaceous glands (the *glands of Zeiss*) and large, coiled sweat glands (the *glands of Moll*) open into the follicles or on the free surface of the border.

The inner surface of the lid is covered by a membrane which has more of the characteristics of a mucous membrane than of an integument. This membrane is called the *conjunctiva*. The surface of the lid which is covered by the conjunctiva is known as the *conjunctival surface*, or because it is the surface directed toward the eyeball, it is called the *ocular surface*. The part of the conjunctiva which lines the inner surface of the lid is known as the *palpebral conjunctiva*. Passing from the lid it extends onto the surface of the eyeball where it forms the *bulbar conjunctiva*. The bulbar conjunctiva consists of two parts: that which lies upon the sclera, the *scleral conjunctiva*, and that which covers the cornea, the *corneal conjunctiva*. As the conjunctival membrane extends from the eyelid to the ocular bulb, it forms an arch between the two, the tissue of which is more or less folded. This arch is known as the *fornix*.

The *stratified squamous epithelium of the palpebral border* continues over the posterior angle of the lid and passes upward on its conjunctival surface for a variable distance, to become a two or three layered stratified columnar epithelium. The goblet cells which are to be found in considerable numbers among the low columnar cells of the free surface of the epithelium, are known as the *mucous cells of Leydig*. The form which the conjunctival epithelium assumes on the inner surface of the lid is continued over the fornix. As it becomes the bulbar conjunctiva it loses its tunica propria and is reduced to a thin, stratified squamous layer. The tunica propria is a layer of delicate connective tissue fibers on which the conjunctival epithelium rests. It contains numerous lymphocytes and small nodules may be present, especially in the region of the fornix.

Internal to the conjunctival surface the connective tissue fibers are closely interwoven and form a firm, compact structure known as the *tarsus* or *tarsal plate*. The inferior border of the tarsal plate lies close to the palpebral border of the lid, its superior border merges gradually with the tissue underlying the conjunctival membrane. The tarsal plate provides a firm support for the lid and also forms a smooth surface for the movement of the lid over the eyeball. The tunica propria is reduced to a thin layer over the plate, the epithelium having the appearance of lying directly upon it.

The tarsal plate contains a number of glands, so arranged that the apertures of their ducts form a row of small openings on the palpebral border just in front of its posterior angle. These glands are known as

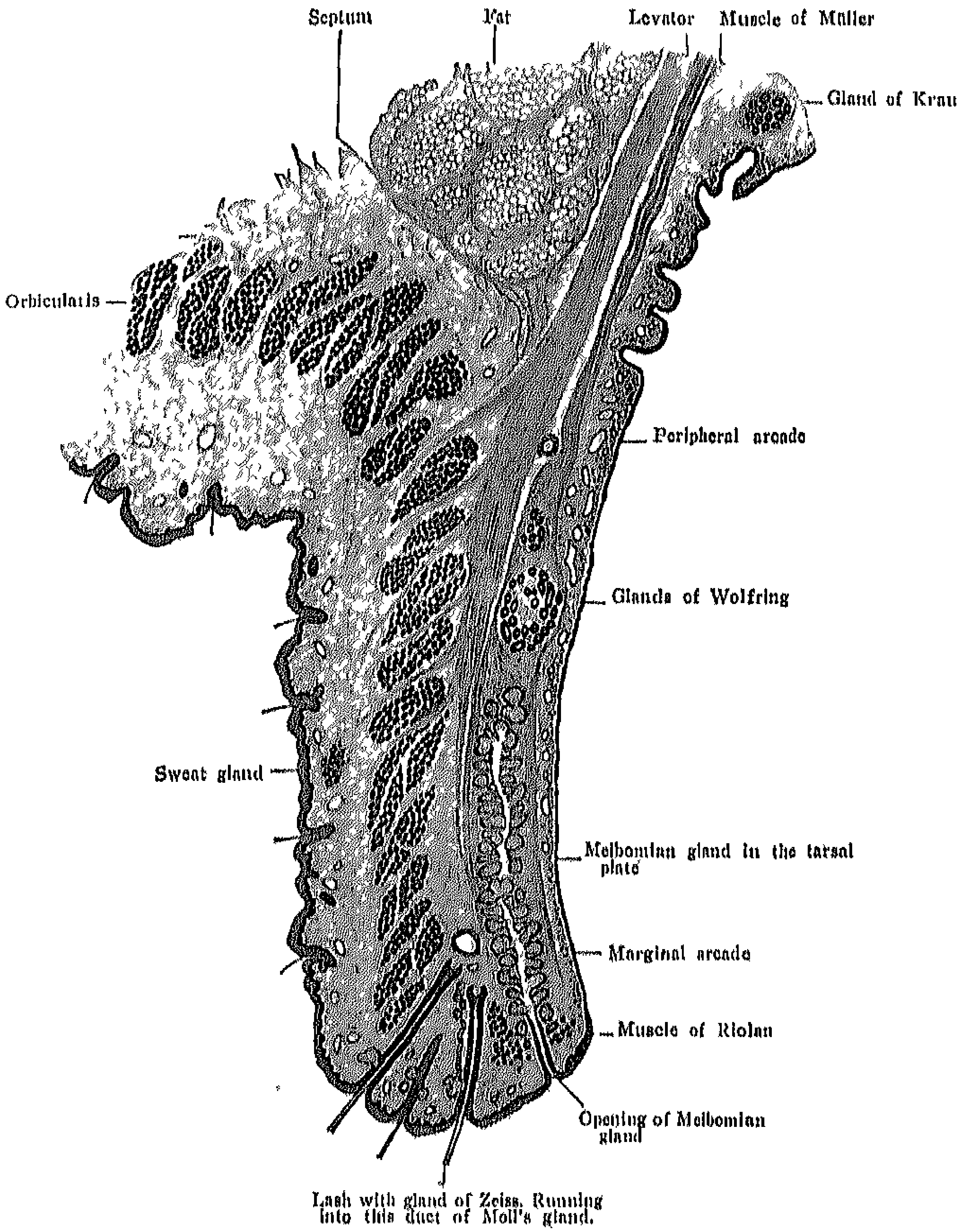


FIG. 275. Vertical section through the upper lid. (Courtesy, Wolff: "The Anatomy of the Eye and Orbit," Philadelphia, The Blakiston Company.)

the *Meibomian glands.* Each gland consists of a duct, lined with stratified squamous epithelium, which extends vertically in the plate, and a number of saccular glands, secreting an oily substance *(sebum palpebrarum),* which are attached to the duct by short necks. The glandular portion of the Meibomian glands closely resembles the sebaceous glands, of which they are a modified form. The oily substance secreted by these glands, lubricates the borders of the lids and also forms a film which prevents the lacrimal fluid from flowing from the conjunctival sac onto the surface of the lid.

Small tubular glands, the *glands of Henle,* are located in the connective tissue above the superior border of the tarsal plate. Groups of serous glands are also located in the connective tissue of the fornix. These are known as the *accessory lacrimal glands* or *glands of Krause.*

A number of striated muscle fibers arranged in bundles which are cut transversely in vertical sections, occupy almost the entire middle portion of the lid *(orbicularis palpebrarum muscle).* These bundles are separated by septa of connective tissue which are continuous with the connective tissue beneath the cutaneous and conjunctival surfaces. A small bundle of these fibers, which has the appearance of being separated from the main portion of the muscle, lies between the roots of the cilia and the tarsal plate. This is known as the *ciliary muscle of Riolan.* Striated fibers from the *levator palpebrae muscle* enter the lid posterior to the orbicularis. The tendinous fibers of the levator muscle are attached to the deep surface of the tarsal plate. They also spread out and, extending between the fiber bundles of the orbicularis muscle, are inserted into the deep surface of the skin. A number of bundles of smooth muscle fibers, the *tarsal muscle of Miller (superior tarsal muscle)* in the upper lid, and *inferior tarsal muscle* in the lower lid, pass from the tendon of the levator palpebrae to the superior border of the tarsal plate.

The blood supply of the eyelid is by vessels which enter at each angle of the eye and by anastomosing, form two arches: a superior tarsal arch, which lies anterior to the upper border of the tarsal plate, and an inferior tarsal arch, which lies in front of the inferior border of the plate. The branches from these arches penetrate the tarsal plate and supply the Meibomian glands. Other branches form capillary networks in the tissue of the conjunctiva, the muscle bundles and the skin. The veins which carry the blood from the lids, join the ciliary vessels in the sclera.

The lymphatics are in the form of networks about the tarsal plate and beneath the skin, their large efferent vessels following the course of the arteries and veins.

The nerves are from the autonomic, sensory and somatic motor centers. The autonomic fibers form networks in the connective tissue beneath the conjunctiva. Fibers from these networks pass to the

Meibomian glands, to the other glands of the eyelid, to the walls of the blood vessels and to the smooth muscle of the tarsae. The sensory fibers lose their myelin sheaths and end freely among the cells of the conjunctival epithelium. Other fibers terminate in end bulbs in the subconjunctival connective tissue. The somatic motor nerves are distributed to the striated fibers of the muscle bundles.

THE LACRIMAL GLANDS

The lacrimal glands are small, oval bodies having a length of about 20 mm. and a breadth of about 12 mm. Their shape resembles that of a small almond. They are located in a depression in the bone of the orbital roof, on the temporal side, which is known as the lacrimal fossa. Instead of being a single gland, each lacrimal gland consists of 8–12 glandular structures which communicate independently with the conjunctival sac. The openings of their ducts form a row of small apertures close to the anterior border of the fornix. The glands are surrounded by a common capsule but are separated by broad septa of connective tissue.

The lacrimal glands produce a watery secretion, the *lacrimal fluid* commonly referred to as "tears," which spreads over the exposed portion of the eyeball keeping it moist and at the same time serving as a lubricant to facilitate the movements of the lids. It also aids in the removal of small particles of dust which have settled on the exposed surface of the eyeball.

In general appearance, the lacrimal glands are similar to the parotid glands, from which they may be distinguished by larger lumina and by the presence of *basket cells (myoepithelial elements)* between the epithelial cells and the basement membrane.

The secreting tubules are of two kinds: those in which the cells of the glandular epithelium are tall and narrow, and those in which the cells are low columnar or cuboidal. The tall cells become shorter after their secretion products have been discharged. In the shorter cells the secretion products are in the form of large, rounded masses, the cytoplasm being confined to the basal portion of the cell. The connective tissue septa by which the two kinds of secreting tubules are separated, contain large numbers of lymphocytes. These two cell types probably represent merely different functional phases of the same cell, the taller cells after discharge of their secretions, shrink and assume the shorter form.

The secreting tubules of each division of the gland are connected by small, intercalated ducts to larger interlobular ducts, which in their turn unite to form the principal excretory duct through which the secretion of the gland is conveyed to the conjunctival sac. The intercalated ducts are lined by a cuboidal epithelium. The epithelium of

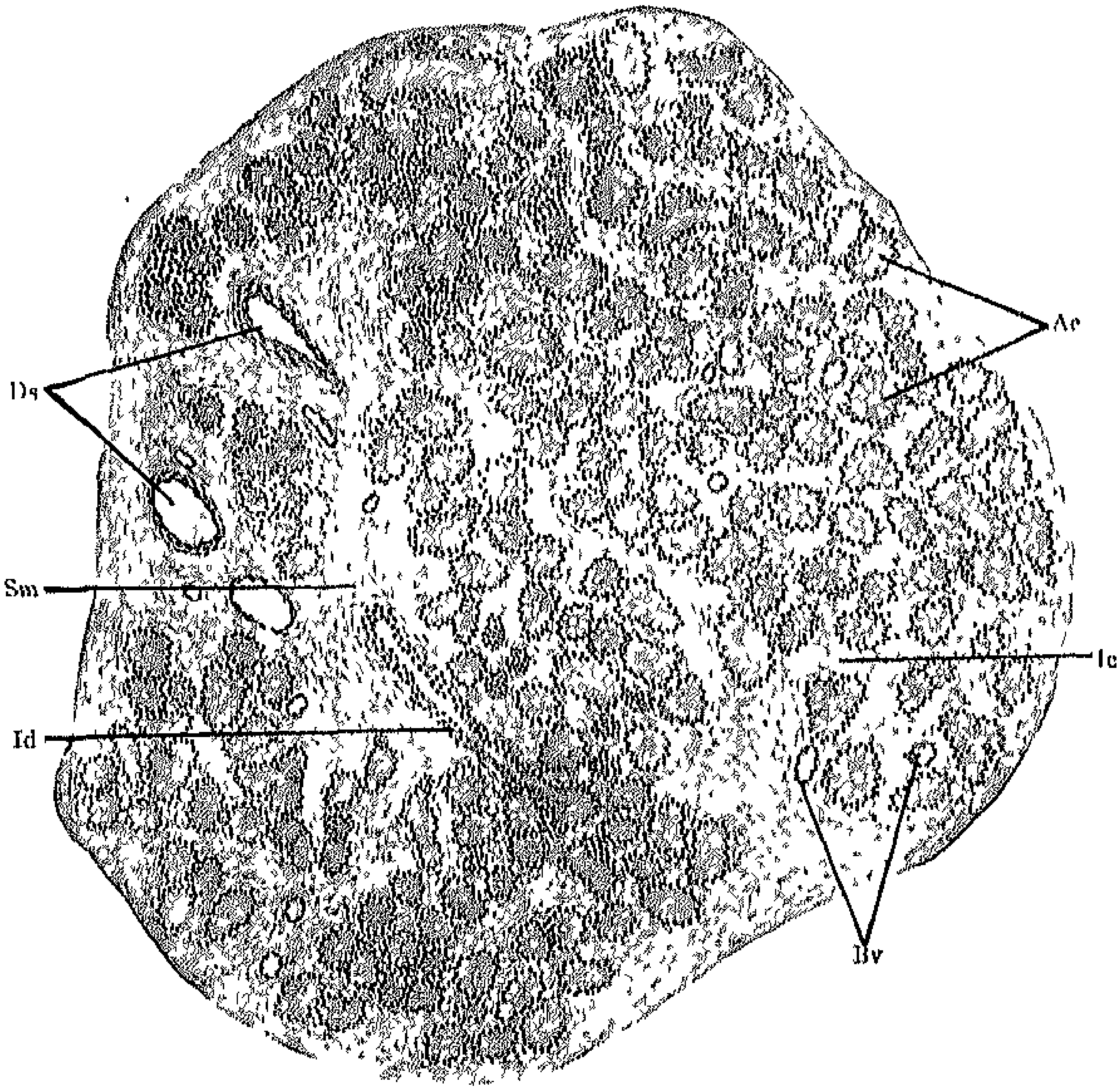


FIG. 276 Section through a lacrimal gland. (Ac) Glandular acini. (Ic) Interstitial connective tissue. (Bv) Blood vessels. (Ds) Ducts. (Sm) Connective tissue septum. (Id) Intercalary duct communicating with several acini.

the interlobular ducts is formed by either cuboidal or low columnar cells. The large excretory ducts are lined by a two layered, columnar epithelium.

The lacrimal fluid leaves the conjunctival sac by the following channels: minute openings, the *lacrimal puncta,* are located at the summits of two conical elevations, the *lacrimal papillae,* near the medial angle of the eye. The puncta lead into two small canals, the *lacrimal canaliculi,* through which the fluid passes to the dilated upper end of the tear duct, the *lacrimal sac.* The *tear duct,* or *nasolacrimal duct,* leads from the lacrimal sac through the bony canal to the point in the inferior meatus where it opens into the nasal cavity.

The canaliculi are lined by a stratified squamous epithelium which rests on a layer of delicate fibrous tissue containing numerous lymphocytes. This layer is called the tunica propria. The tissue which surrounds the tunica propria is well supplied with elastic fibers. The lacrimal sac and the nasolacrimal duct are both lined with a two-layered columnar epithelium, some of the cells of which are supplied with cilia. The epithelium of these channels rests on a delicate tunica propria in which a large number of lymphocytes are present. The loosely arranged connective tissue which lies between the ducts and the periosteum of the surrounding bone. contains a rich plexus of blood vessels.

The *accessory lacrimal glands (Krause's glands)* have already been described (see p. 480). They are small, compound tubular glands located in the connective tissue which lies beneath the epithelium of the fornix, their position being toward the medial (nasal) angle of the eye.

23

The Ear

The ear is the organ of hearing, and a portion of it is differentiated to receive proprioceptive stimuli concerned with equilibrium. By location it is divided into three parts: the *external ear,* the *middle ear,* and the *internal ear.*

The external ear consists of the *auricle* or *pinna,* which is an irregularly shaped, flaplike appendage attached to the side of the *external auditory meatus,* which is closed internally by the *tympanic membrane* or *ear drum.*

The middle ear is an irregular cavity in the temporal bone. It is separated laterally from the external ear by the tympanic membrane. Anteromedially it connects with the nasopharynx by way of the *Eustachian (auditory) tube.* It contains three small bones, the *auditory ossicles,* which transmit the vibrations caused by sound waves striking against the tympanic membrane to the structures of the inner ear.

The inner ear consists of a complex arrangement of membranous sacs and tubes which constitute the membranous labyrinth. In certain restricted areas in the membranous labyrinth, occur specialized neuroepithelial elements which receive the stimuli for both sound and equilibrium and initiate the impulses which are transported by way of the auditory and vestibular nerves, respectively, to the brain. The membranous labyrinth is enclosed within cavities in the petrous portion of the temporal bone, which conform in a general way to the shape and arrangement of the structures of the membranous labyrinth. These cavities in the bone form the *bony (osseous) labyrinth.*

THE EXTERNAL EAR

The structures of the external ear, the *auricle* and *external auditory meatus,* collect the sound waves and convey them to the point where they impinge on the tympanic membrane.

The auricle is a large flattened fold of skin supported by a plate of elastic cartilage. Its anterior surface is moulded into a number of folds and ridges by the irregularities of the cartilage. Its posterior surface is convexly curved to correspond to the concavity of its anterior

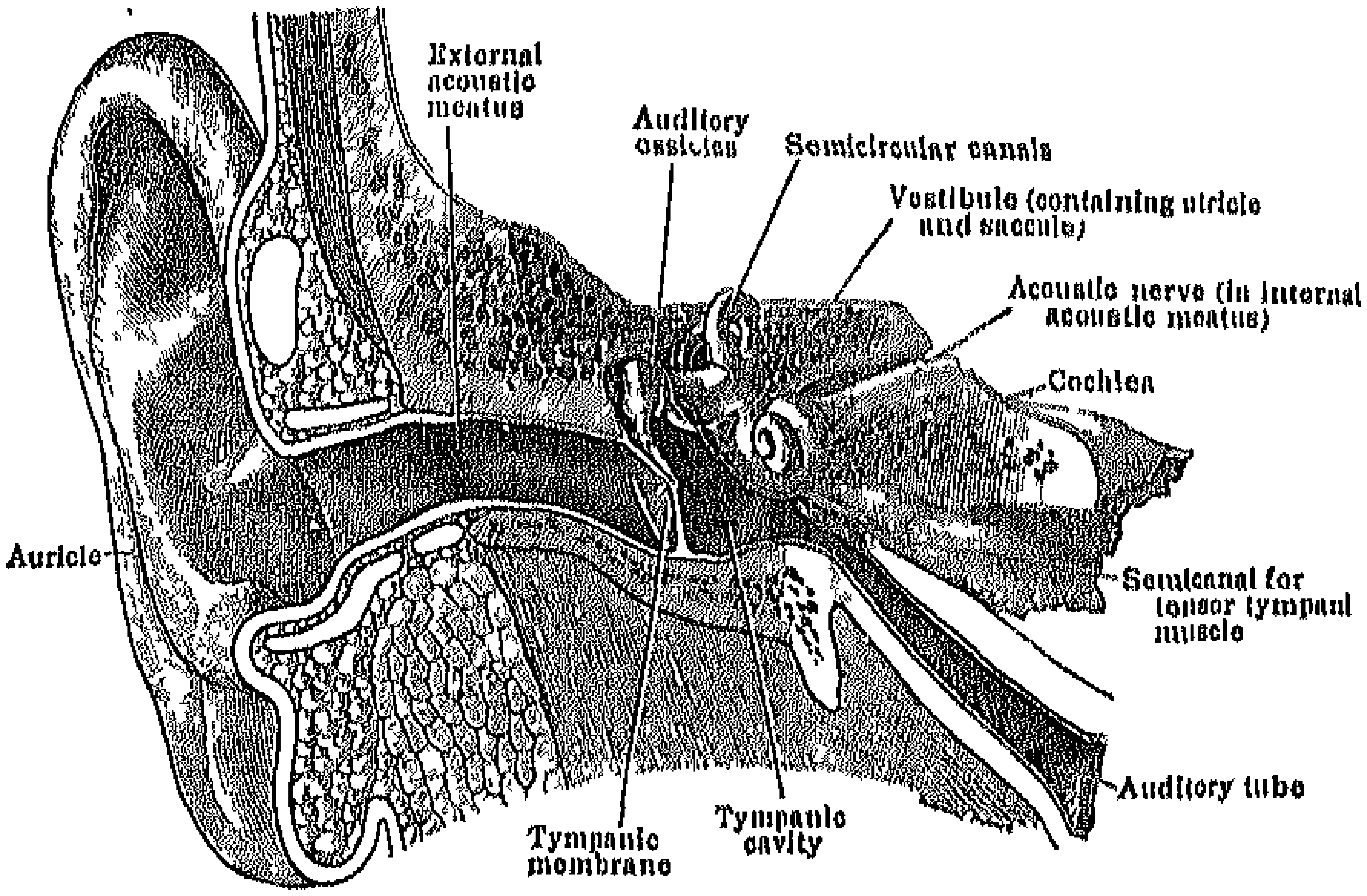

External acoustic meatus
Auditory ossicles
Semicircular canals
Vestibule (containing utricle and saccule)
Acoustic nerve (in internal acoustic meatus)
Cochlea
Auricle
Semicanal for tensor tympani muscle
Auditory tube
Tympanic membrane
Tympanic cavity

FIG. 277. Dissection of the right ear, anterior half removed. Natural size. (Courtesy, J. Parsons Schaeffer, Ed.: "Morris' Human Anatomy," Philadelphia, The Blakiston Company.)

surface. The skin covering its surfaces is exceedingly thin and is attached directly to the perichondrium anteriorly, a layer of subcutaneous connective tissue being interposed between it and the perichondrium on the posterior surface. The skin covering the auricles is provided with a number of delicate hairs, associated with which are small sebaceous glands. A few small sweat glands are present on the posterior surface of the ear.

The *external auditory meatus* is a slightly twisted canal which extends from its external opening to the tympanic membrane. A plate of cartilage, continuous with the cartilage which supports the auricle, surrounds its outer third. This cartilage is incomplete in its upper, posterior portion, thus providing an approach for the blood vessels and nerves which supply the structures of the external ear. The inner two-thirds of the external meatus is located in the lateral portion of the temporal bone.

The skin which covers the auricle is continued into the meatus and forms its lining. It is relatively thick in the cartilaginous portion. In the bony portion the corium merges with the periosteum, except in the thickened area which covers the roof.

In the outer part of the meatus the skin bears a number of fine hairs. The hairs in the bony portion of the canal are confined to the tissue that lines the roof. A number of large, stiff hairs are present near the external opening of the meatus and they guard against the entrance

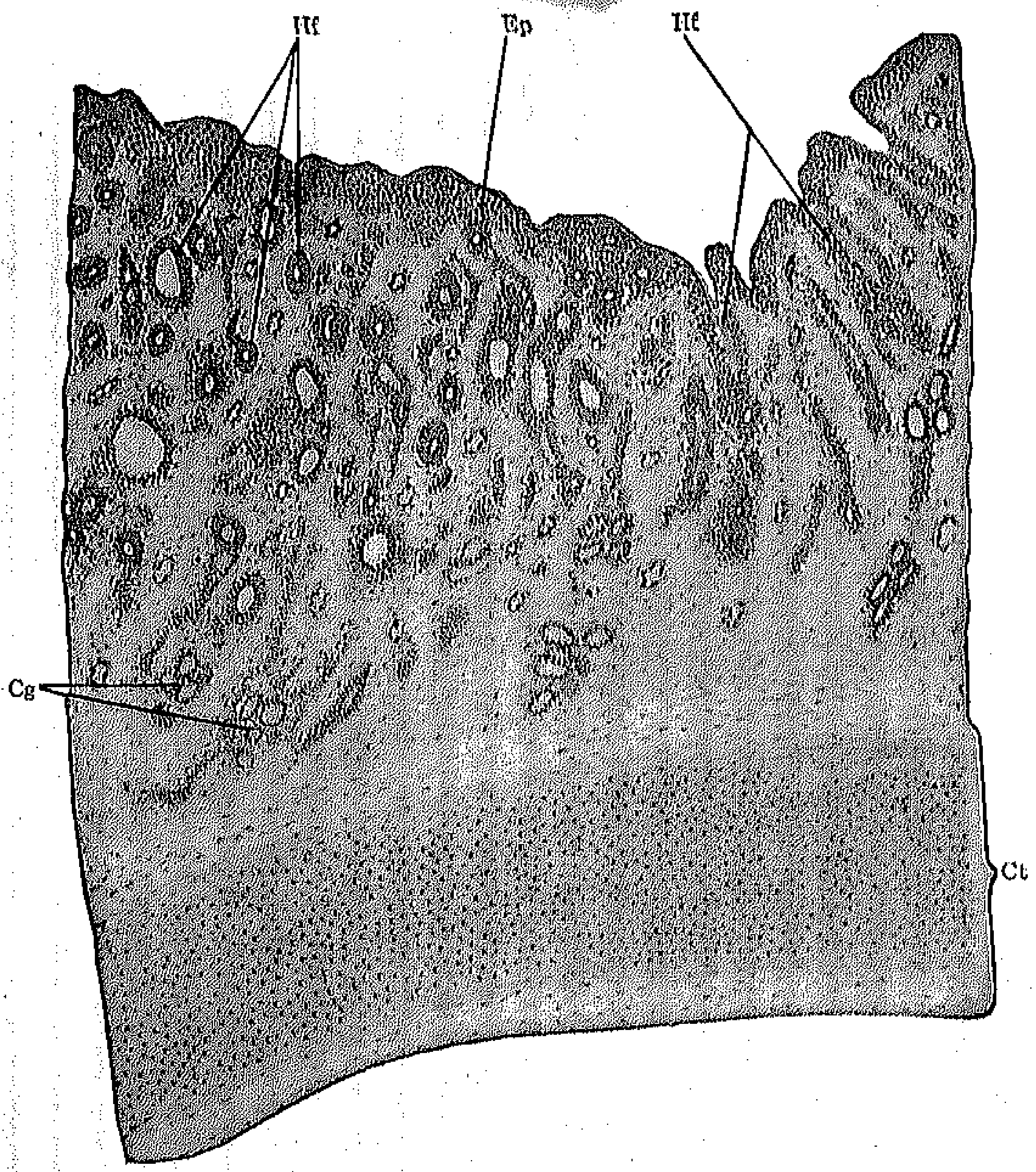


FIG. 278. Section through a portion of the wall of the external auditory canal. (Ep) Epithelial lining of the canal. (Hf) Hair follicles. (Cg) Ceruminous gland. (Ct) Elastic cartilage.

of foreign bodies into the ear. Associated with the hairs are large sebaceous glands and numerous coiled tubular glands, known as the *ceruminous glands.* These glands are modified sweat glands. They produce a secretion which has a yellowish color, due to the presence of brownish pigment granules and fat droplets. This secretion, mingled with the secretion of the sebaceous glands and desquamated epithelial cells, forms the *cerumen* or ear wax.

Blood vessels entering through the fissure in the upper, posterior part of the cartilage, break up into capillaries which are distributed to the perichondrium, the periosteum, the hair follicles, and the glands.

The nerves are from the autonomic system to the blood vessels and glands; sensory fibers supply the skin.

THE MIDDLE EAR

The middle ear or *tympanic cavity* is an irregular space in the temporal bone between the wall of the bony labyrinth medially and the tympanic membrane laterally. The cavity is filled with air which enters through the Eustachian tube by means of which the tympanic cavity communicates with the nasopharynx. Posteriorly it communicates, by way of the tympanic antrum, with the air cells of the mastoid process of the temporal bone. The structures included in the tympanic cavity are the *auditory ossicles;* the *tensor tympani* and *stapedius,* two small muscles which, by their contractions regulate the movements of the ossicles; and the *chorda tympani,* a small branch of the facial nerve. The tympanic cavity and the structures it contains are all covered by a mucous membrane. The tympanic membrane separates the middle ear from the external acoustic meatus.

The medial wall of the tympanic cavity (lateral wall of the bony labyrinth) is pierced by two small openings or "windows": the *fenestra ovalis (fenestra vestibuli)* and the *fenestra rotunda (fenestra cochlea).* The fenestra ovalis lies between the tympanic cavity and that portion of the bony labyrinth known as the *vestibule.* The fenestra rotunda lies between the tympanic cavity and the *scala tympani.*

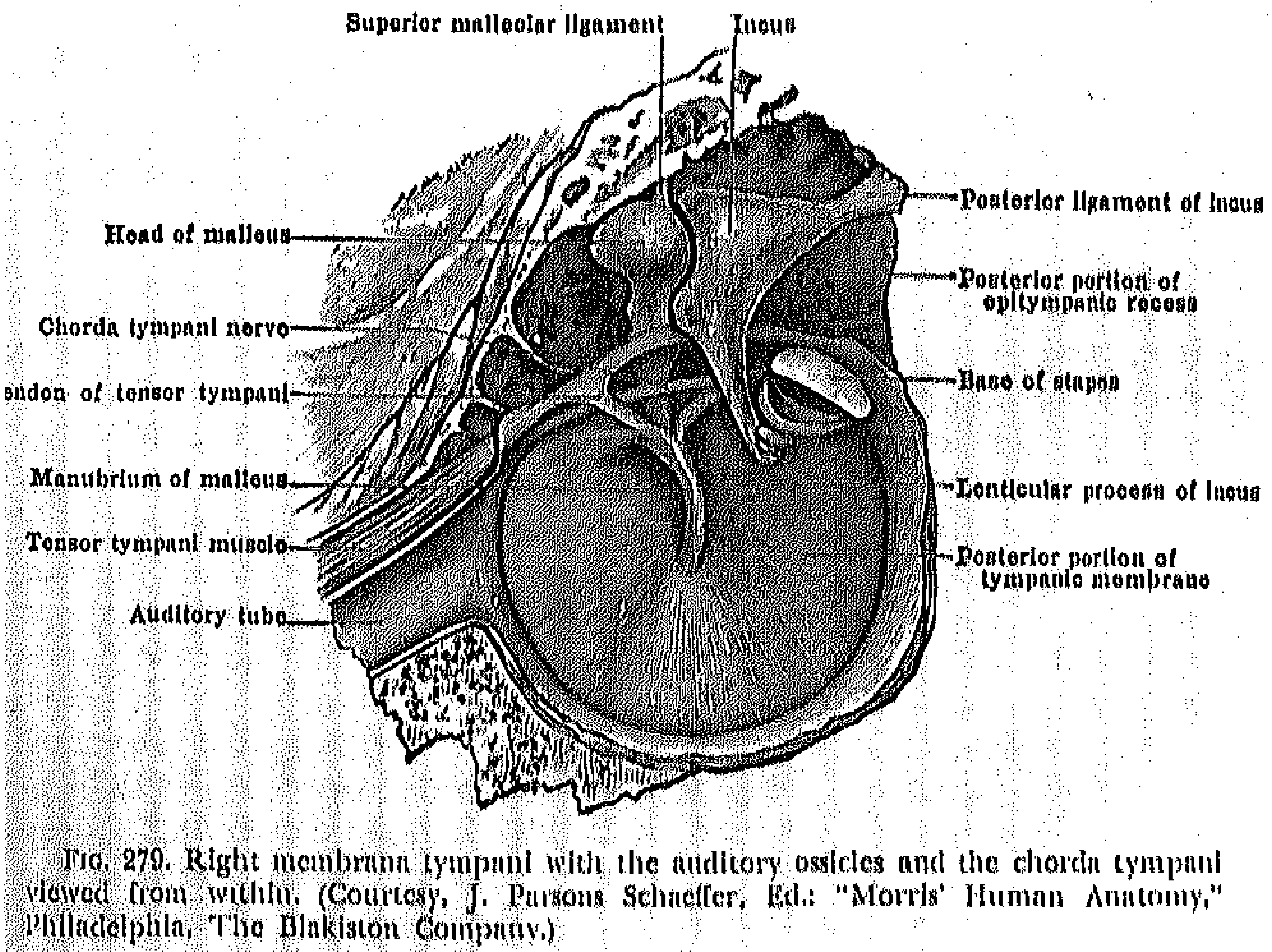

Superior malleolar ligament
Incus
Posterior ligament of incus
Head of malleus
Posterior portion of epitympanic recess
Chorda tympani nerve
Base of stapes
endon of tensor tympani
Manubrium of malleus
Lenticular process of incus
Tensor tympani muscle
Posterior portion of tympanic membrane
Auditory tube

Fig. 279. Right membrana tympani with the auditory ossicles and the chorda tympani viewed from within. (Courtesy, J. Parsons Schaeffer, Ed.: "Morris' Human Anatomy," Philadelphia, The Blakiston Company.)

The auditory ossicles are three small bones, the *malleus,* the *incus,* and the *stapes.* These bones are made up of typical compact bone covered by periosteum except over their articular surfaces. A marrow cavity is not present in either the malleus or the incus, but is found in the stapes. The malleus is attached to the inner surface of the tympanic membrane by a slender process, the *manubrium.* The head of the manubrium articulates with an articular facet on the body of the incus. The lenticular process of the incus articulates with the head of the stapes. The expanded foot plate of the stapes is set into the fenestra ovalis and is held in place by a fibrous and elastic membrane called the *stapedial ligament.* The function of the ossicles is to transmit vibrations (produced by the action of sound waves striking the tympanic membrane) to the perilymph of the inner ear.

The tensor tympani muscle (striated muscle) lies in a bony canal above the Eustachian tube. A fibrous septum separates the muscle from the tube. The muscle inserts into the upper part of the manubrium of the malleus by means of a slender tendon which makes a sharp turn as it leaves the bony canal in order to reach the malleus. The stapedius muscle (also striated muscle) arises within the pyramidal eminence. A small opening at the apex of the eminence allows emergence of the slender tendon of the muscle which inserts on the neck of the stapes. The tensor tympani muscle maintains the tension of the tympanic membrane, while the stapedius, by its contraction, increases the pressure on the perilymph of the inner ear, thus acting to damp loud sounds or noises.

The chordi tympani is a branch of the facial nerve which crosses the tympanic cavity on the inner surface of the tympanic membrane and over the manubrium of the malleus. It is also covered by the mucous membrane lining the cavity.

The mucous membrane which forms the lining of the tympanic cavity consists of a layer of thin, flattened squamous cells resting on a delicate fibrous layer, the tunica propria. Where the mucous membrane lies upon the bony wall of the cavity, the subepithelial connective tissue merges directly with the periosteum. The membrane lining the cavity is continued over the surfaces of the auditory ossicles and their muscles. Through the antrum it is also continuous with the mucous lining of the mastoid cells. The cells which form the epithelium about the opening of the cavity into the Eustachian tube may be cuboidal or low columnar and are frequently provided with cilia.

The *tympanic membrane* is a thin, semitransparent structure nearly oval in outline, being somewhat broader in its upper than in its lower part. It is supported by a ring of bone containing a deep groove, the *sulcus tympanicus,* in which the thickened border of the membrane, the *annulus fibrosus,* is set. The bony ring which supports

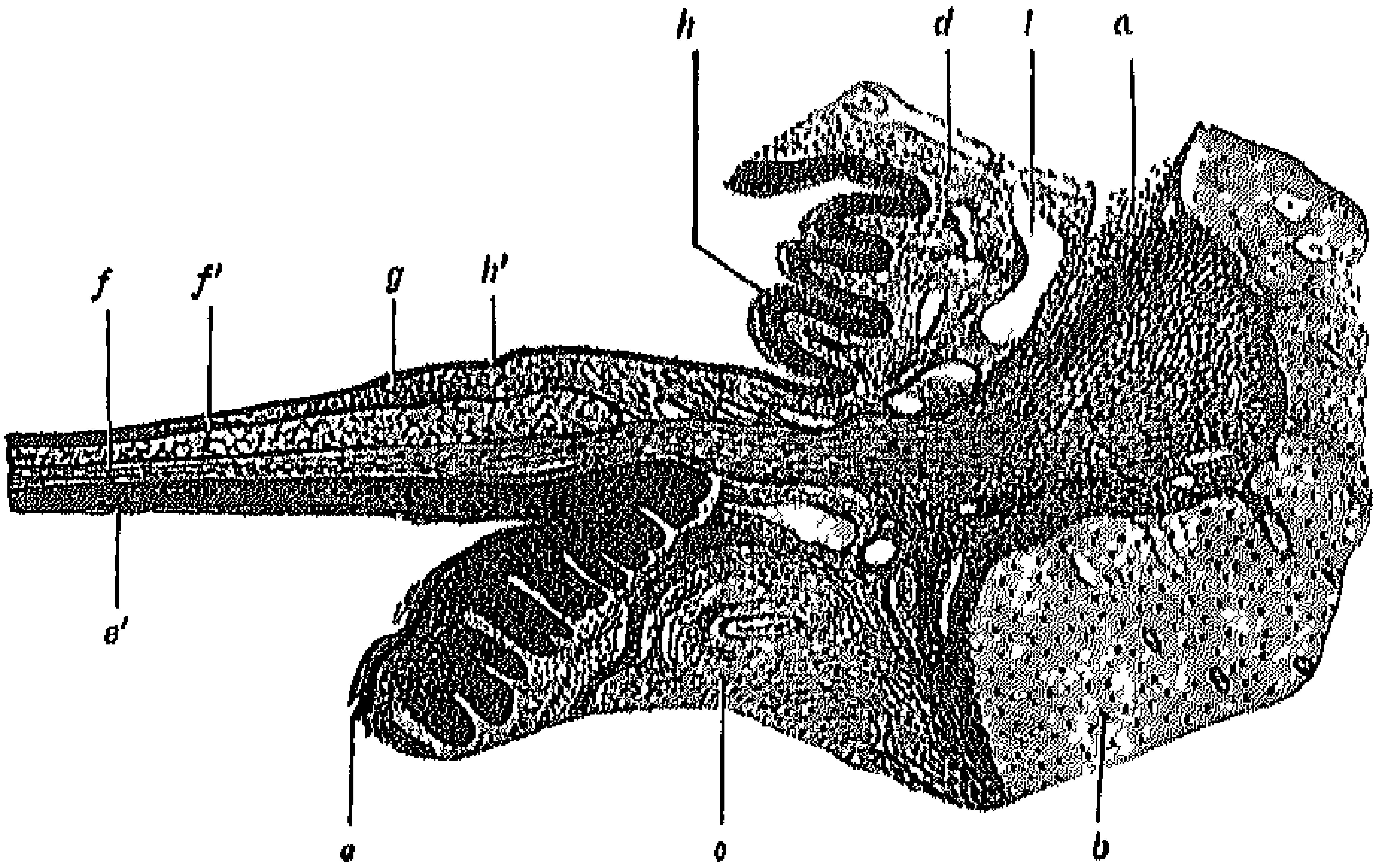


FIG. 280. Cross section of the edge of the tympanic membrane of a child. *(a)* Fibrocartilaginous ring. *(b)* Bone. *(c)* Skin with papillae. *(d)* Mucous membrane of tympanic cavity. *(e)* Epidermis of the external meatus. *(e')* Epidermis of the tympanic membrane. *(f)* Radial fibers. *(f')* Circular fibers of the tympanic membrane. *(g)* Mucosa of the tympanic membrane. *(h')* Its squamous epithelium. *(h)* Ciliated columnar epithelium of the tympanic cavity. *(i)* Vessels. (Redrawn from v. Ebner.) (After Maximow and Bloom.)

the tympanic membrane is incomplete in its upper part, forming a hiatus in the bone known as the *notch of Rivinus*. Two folds arise from the borders of the notch and enclose a triangular area, the apex of which is toward the center of the membrane. The portion of the membrane in this area is loosely arranged and is known as the *pars flaccida* or *membrane of Shrapnell*. The remainder of the membrane is tightly stretched and is known as the *pars tensa*.

The attachment of the manubrium extends from the apex of the pars flaccida to the center of the membrane which is pulled inward so that its outer surface presents a slight concavity. The deepest point in this concavity is where the flattened extremity of the manubrium is attached. This point is known as the *umbo*.

The tympanic membrane consists of three layers: an external or *cutaneous* layer, a middle or *fibrous* layer, and an internal or *mucous* layer.

The cutaneous layer is continuous with the skin which forms the lining of the external auditory meatus. It consists of an extremely thin stratum of stratified squamous epithelium, the *epidermis*, which is supported by a thin layer of subepithelial connective tissue called the *corium*. The corium is poorly developed and so blends with the tissue of the fibrous layer that it can be distinguished only with difficulty. The epithelium on the outer surface of the tympanic membrane is not papillated.

The fibrous portion or *substantia propria* consists of collagenous tissue with an intermingling network of delicate elastic fibers, the elastic tissue being most abundant toward the central part of the membrane. It presents two layers: an outer layer in which the fibers are radially arranged, diverging as they pass from the umbo to the periphery of the membrane, and an inner layer of circularly arranged fibers which are in the form of a series of concentric rings. These fibers, particularly the radial fibers, combine to form a thickened rim at the periphery of the membrane, the *annulus fibrosus*, which is attached to the groove on the ring of bone by which the membrane is supported. Numerous connective tissue cells occur between the fibers of both layers.

The mucous layer which lies on the inner surface of the tympanic membrane consists of thin, flattened cells; between the cells and the fibrous layer is a thin substratum of connective tissue. The mucous layer is continuous with the mucous membrane which forms the lining of the tympanic cavity.

Blood is supplied by the branches of arteries in the external meatus and tympanic cavity. These vessels enter the thickened periphery of the membrane and form vascular nets on its inner and outer sides. These vascular nets are connected by small branches which pass from one to the other through the substance of the membrane. Branches pass downward in the substantia propria and are distributed among its fibers. The veins follow, in general, the course of the arteries and communicate with the larger vessels in the external meatus and the tympanic cavity.

The nerves enter the substantia propria along with the vessels and pass to the mucous and cutaneous surfaces, beneath which they form delicate plexuses.

The innervation of the tympanic membrane is mainly by way of the auriculotemporal branch of the mandibular nerve, supplemented by the auricular branch of the vagus and the tympanic branch of the glossopharyngeal. These nerves transmit sensory (pain) sensation and also accompany and supply sympathetic fibers to the blood vessels of the drum.

The *Eustachian* or *auditory tube (tuba auditiva)* extends from the lateral wall of the nasopharynx to the anterior part of the tympanic cavity. Its upper third, which passes through a bony canal, is known as the *bony portion* of the tube. Its lower two-thirds is partly surrounded by cartilage and partly by fibrous tissue, and constitutes the *cartilaginous portion*. The cartilage lies on the posterior wall and

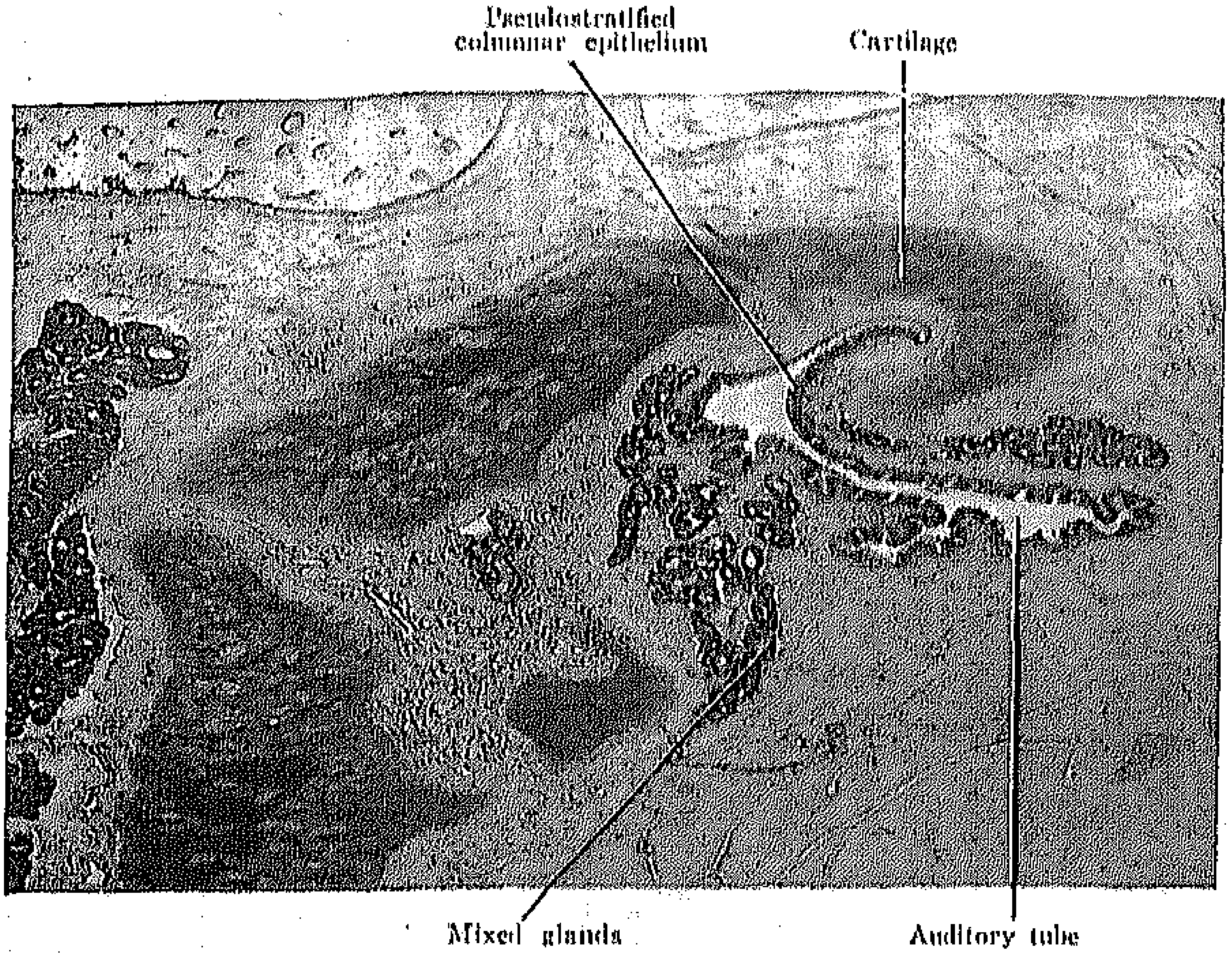


FIG. 281. Section through the cartilaginous portion of the auditory tube. Photomicrograph.

curves around the outer side of the tube in a manner that suggests the form of a fish hook when viewed in transverse section. When projected lengthwise, the cartilage will be understood to form a groove in which the Eustachian tube lies.

In its lower part the Eustachian tube is lined by a stratified columnar (pseudostratified) epithelium. The epithelium of the upper part of the cartilaginous portion of the tube consists of tall columnar cells which change to low columnar in the bony portion, and may even be cuboidal close to the opening of the tube into the tympanic cavity. Goblet cells are numerous and they form the lining of simple depressions in the epithelium. The cells of the tubal epithelium are usually ciliated.

The epithelium rests on a thick layer of fibroelastic tissue, which contains numerous mucous secreting glands. The subepithelial tissue in the bony portion of the tube is quite thin and merges directly with the periosteum of the bone. Only a few small mucous glands are present. The thick subepithelial tissue which surrounds the opening of the tube into the nasopharynx contains large masses of lymphoid tissue, the *tubal tonsils*.

The *levator palati* and *tensor palati muscles* are both associated with the Eustachian tube. The levator palati muscle is located below and a little toward the inner side, while the tensor palati muscle is located on the outer side. The attachment of these muscles to the cartilage is such that they act as dilators of the tube.

THE INTERNAL EAR

The internal ear is located in the petrous portion of the temporal bone and consists of a bony and a membranous labyrinth, the latter enclosed in the former. The membranous labyrinth encloses the endolymph space which contains a fluid called *endolymph*. The space between the wall of the bony labyrinth and the membranous structures it contains is known as the perilymph space and likewise contains a fluid, the *perilymph*. The bone which borders the bony labyrinth is of a different texture from that of the temporal bone. The inner layer, formed by the endosteum lining the bony labyrinth, is extremely dense and is avascular. Next is an intermediate layer which grades from an extremely hard bone on its inner margin to a less dense bone on its outer margin. This layer is endochondral bone and it contains clusters of embryonal cartilage which persist throughout life. The outer layer is less dense bone, similar to that of the outer margin of the middle layer. It is derived from the periosteum. These three layers of bone form what is known as the osseus capsule. It is possible, by careful dissection, to remove the osseous labyrinth intact. This is especially the

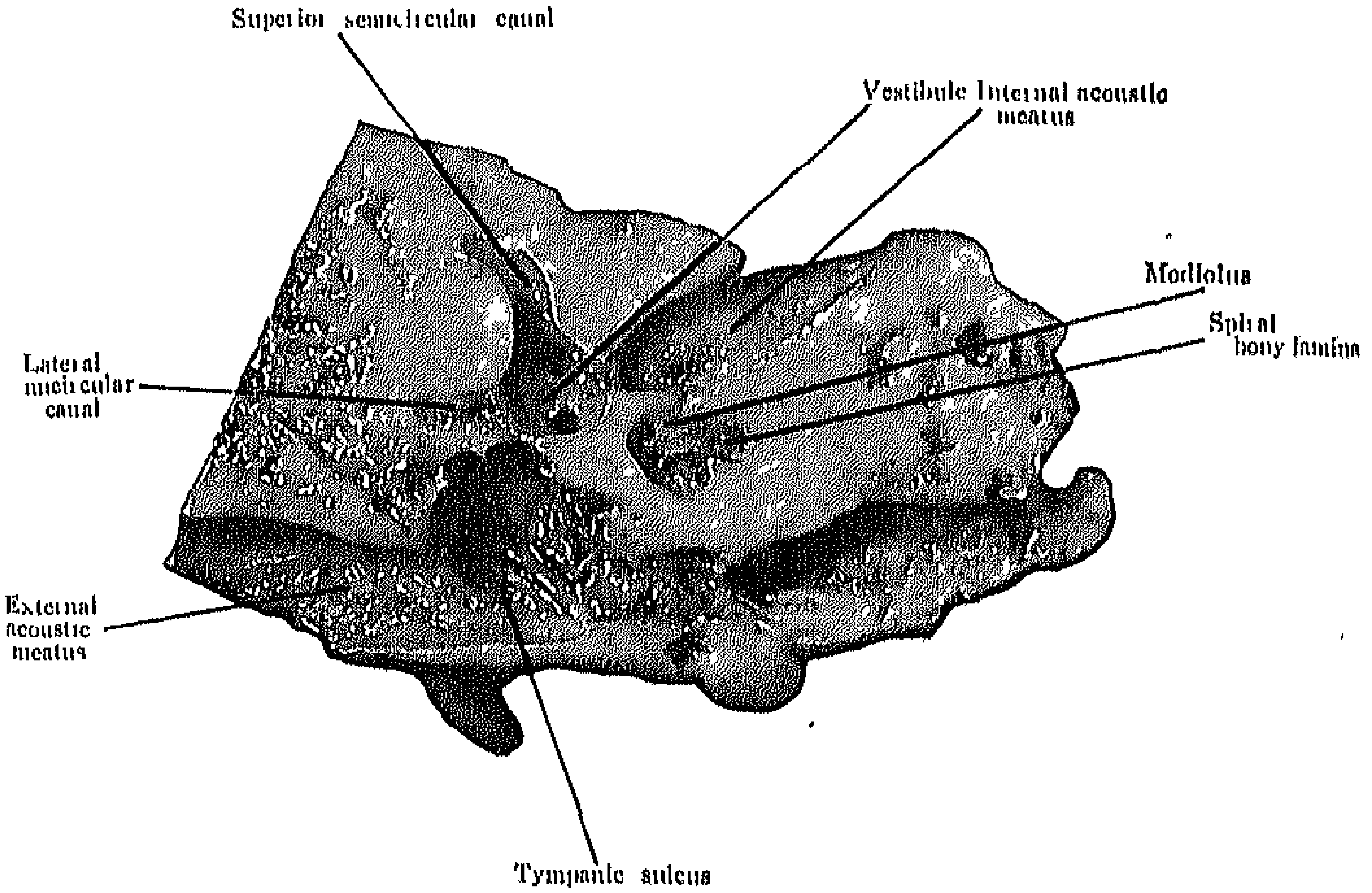


FIG. 282. Transverse section through the right temporal bone, lower half, viewed from above.

case in young infants; in older persons the difference in the hardness of the bone is not so great.

THE BONY LABYRINTH. The bony or osseous labyrinth consists of a central cavity, the *vestibule,* three canals, the *semicircular canals* which open into the vestibule, and a spirally wound tube, the *cochlea,* which likewise communicates with the vestibule.

The vestibule is a large oval cavity separated from the tympanic cavity by a thin plate of bone. Two openings are located in this bone: the round window, which is covered by a membrane, the secondary tympanic membrane; and the oval window, closed by the foot plate of the stapes. The foot plate is held in place by the stapedial ligament which consists of collagenous and elastic fibers extending from the border of the foot plate to the margin of the window. Both the foot plate and the oval window are rimmed with cartilage.

The medial wall of the vestibule is marked by two depressions, one of which is occupied by the *utricle,* the other by the *saccule.* Posteriorly, it communicates with the semicircular canals and anteriorly with the cochlea. A canal, the *vestibular aqueduct,* leads from its medial wall to the posterior surface of the petrous portion of the temporal bone. It contains the *ductus endolymphaticus* (a part of the membranous labyrinth).

The three semicircular canals are known as *superior, lateral,* and *posterior,* according to the plane in which they lie. The lateral canals, on either side of the head, lie in the same plane. The superior canal of one side and the posterior canal of the opposite side occupy approximately parallel planes. The lateral end of the superior canal, the anterior end of the lateral canal, and the lower end of the posterior canal form enlargements or ampullae where they open into the vestibule. The medial end of the superior canal and the upper end of the posterior canal unite to form a single trunk, the *crus commune,* through which they communicate with the vestibule. Thus there are three openings by means of which the canals communicate with the vestibule.

The cochlea which forms the anterior part of the bony labyrinth resembles the shell of a garden snail in the manner in which it makes two and one-half spiral turns about a conical, central pillar, the *modiolus.* A thin shelf, the *bony spiral lamina,* projects from the side of the modiolus into the cochlear canal. When this is completed by the addition of the *membranous spiral lamina (basilar membrane),* which extends from the free border of the bony lamina to the outer wall of the canal, a partition is formed that divides the canal into an upper and lower part. The upper part is again subdivided by a delicate membrane, which passes downward and medially from the outer wall. Thus three compartments, an upper, an intermediate and a lower, are formed in the cochlear canal. Each of these compartments begins at the base of the modiolus and follows the spiral turns of the cochlea to its apex.

The upper compartment is known as the *scala vestibuli* and communicates through a small opening with the vestibule. The lower compartment is called the *scala tympani*, the basal portion of which is shut off from the tympanic cavity by a fibroelastic membrane that fills the fenestra rotunda. This membrane is sometimes referred to as the *secondary tympanic membrane*. The scala vestibuli and scala tympani communicate by means of a small aperture at the summit of the cochlea, the *helicotrema*. The intermediate compartment is separated from the scala vestibuli by the *thin membrane of Reissner* and from the scala tympani by the *basilar membrane*, and forms the *cochlear*

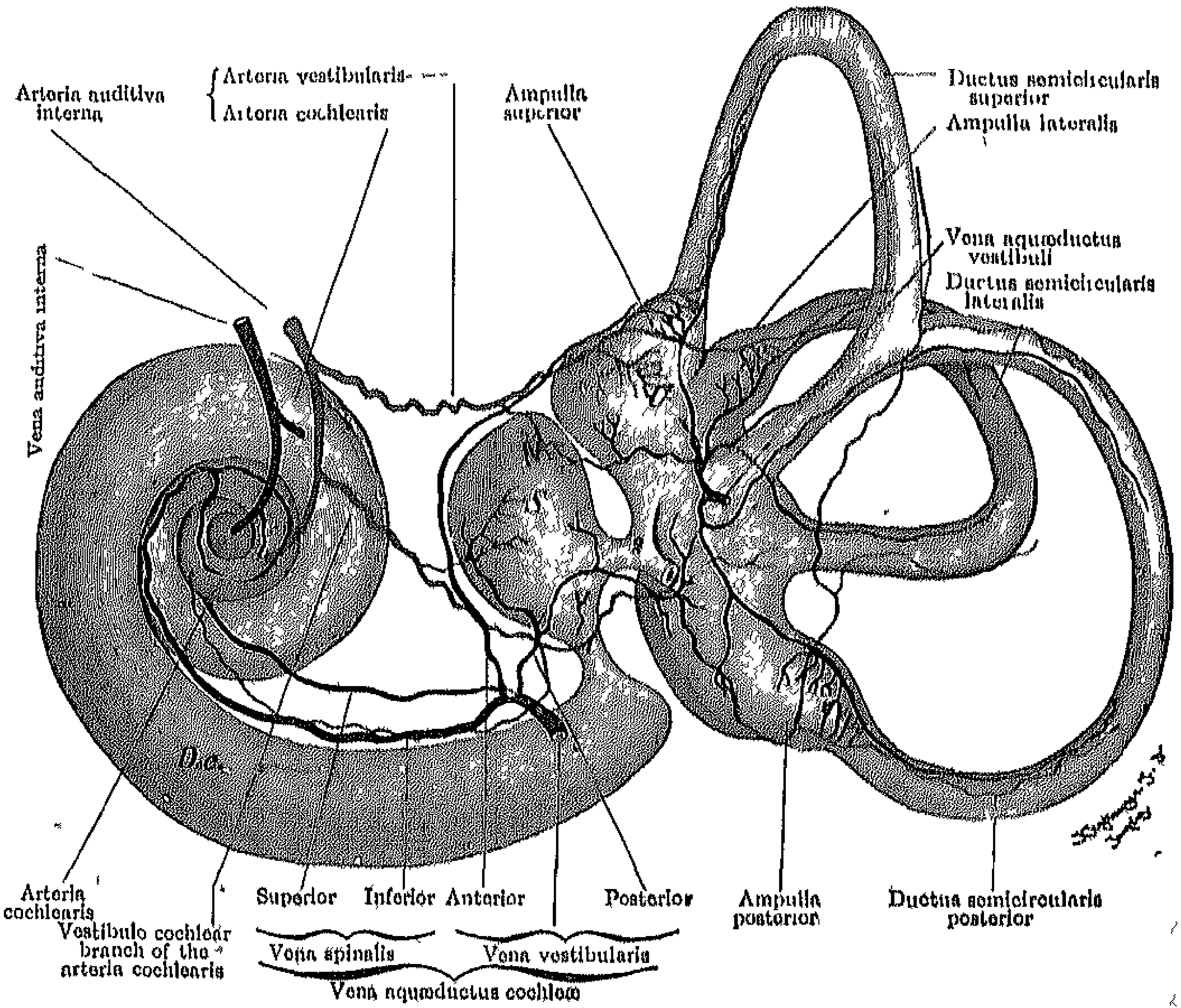


FIG. 283. Diagram of the blood vessels of the right human labyrinth. Medial and posterior aspect *(D.c.)* Ductus cochlearis. *(S)* Sacculus. *(U)* Utriculus. *(1)* Ductus reuniens. *(2)* Ductus utriculo-saccularis The saccus endolymphaticus is cut off. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

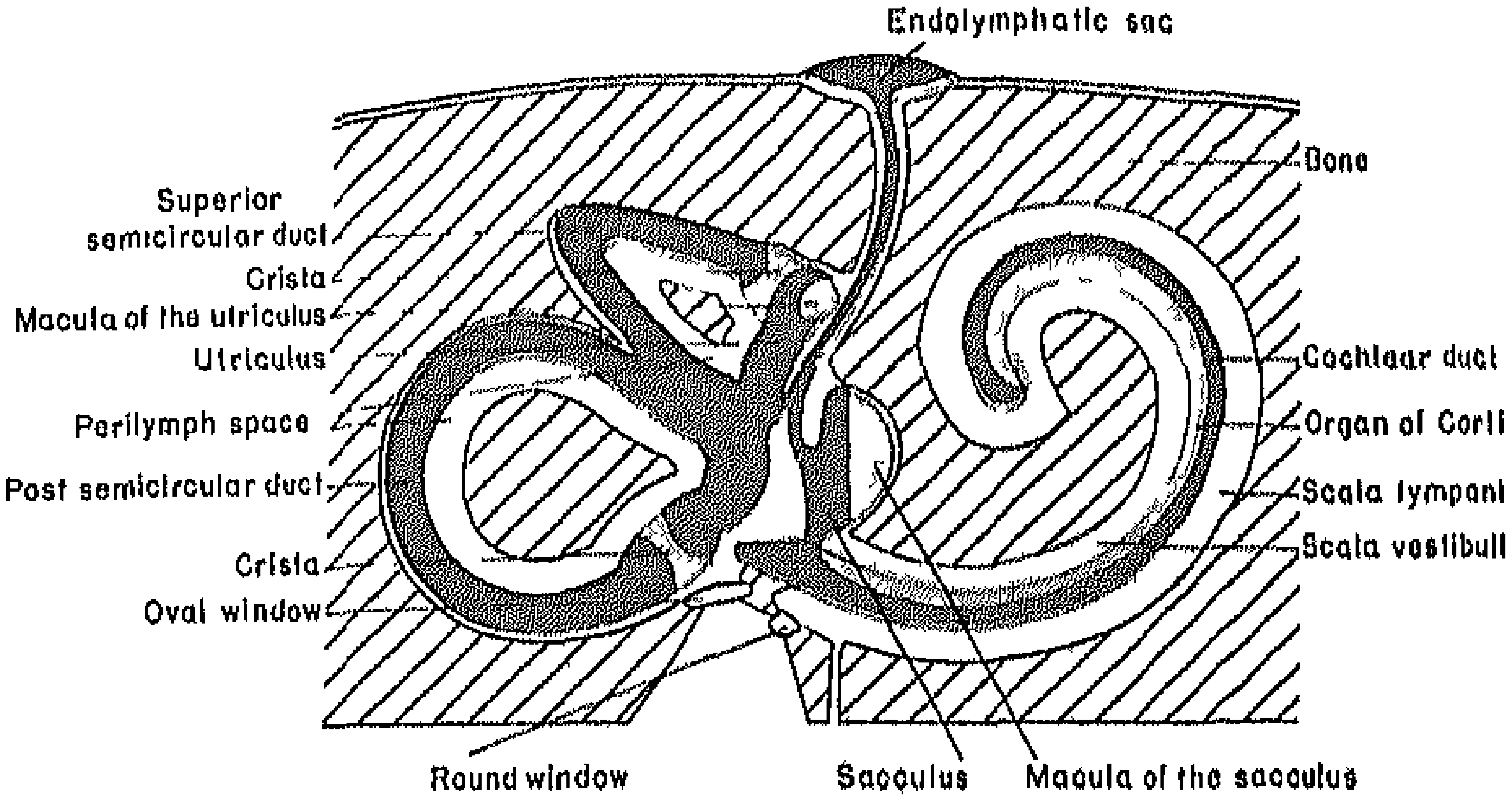


FIG. 284. Scheme of right bony and membranous labyrinth. The neuro-epithelial areas (yellow) are shown in their relation to the membranous labyrinth (red).

duct. The upper and lower compartments, the scalae, contain perilymph, while the middle compartment, the cochlear duct, contains endolymph.

The osseous labyrinth is lined by a delicate layer of endosteal tissue. This is covered by mesenchymal epithelial cells which form the immediate lining of the perilymph space and secretes the perilymph. The perilymph and endolymph are each contained in closed systems and do not mix.

THE MEMBRANOUS LABYRINTH. The membranous labyrinth consists of a series of intercommunicating sacs and canals whose shape and arrangements conform, in a general way, to that of the bony labyrinth. Two saclike structures, the *utricle* and the *saccule*, are located in the vestibule. The utricle occupies its upper, posterior part, while the saccule is found in the lower, anterior part. The utricle and saccule are united by the Y-shaped *utriculosaccular duct* which continues as the *ductus endolymphaticus*, a slender, membranous canal located in the vestibular aqueduct. It continues to the posterior surface of the temporal bone, where its dilated end forms the *endolymphatic sac* which lies between the bone and the dura mater. The membranous semicircular canals open into the utricle while the cochlear duct is united to the saccule by way of a very short slender duct *(ductus reuniens)*.

From the foregoing it is clear that the endolymph is continuous throughout the membranous labyrinth. Whether it flows freely from one part of the labyrinth to the other is doubtful, however.

The walls of the membranous canal, barring those areas in which the neuroepithelial elements are located, consist of two layers: an outer layer composed of delicate connective tissue fibers among which are numerous branched, pigmented connective tissue cells, and an inner epithelial layer of ectodermal origin, consisting of flattened squamous cells. This inner epithelial layer rests on a clearly defined basement membrane. In the semicircular canals, trabeculae consisting of bundles of connective tissue fibers extend from the periosteal layer to the fibrous outer portion of the wall of the membranous labyrinth. The mesenchymal epithelial cells which form the lining of the perilymph space are continued about the trabeculae and over the outer surfaces of the membranous labyrinth that are exposed to the perilymph.

A portion of the epithelial lining of the utricle and saccule, and of the ampullae of the semicircular canals, is transformed into neuroepithelial structures known as the *maculae* and *cristae*. The neuroepithelium of the cochlear duct forms a complex structure known as the *organ of Corti*.

THE MACULAE. According to their location, the maculae are known as the *macula utriculi* and the *macula sacculi*. They are thickened areas about 3 mm. long and 2 mm. broad. The fibrous tissue of the periosteum is considerably increased in the region of the maculae. This supports a modified epithelium which consists of two types of cells, the *sustentacular cells* and the *sensory* or *hair cells*. The sustentacular cells are tall columnar elements, having broad, proximal portions which rest on the basement membrane, and narrow distal portions which reach to the surface of the epithelium. The light staining, vesicular nuclei are oval in outline and are located in the basal

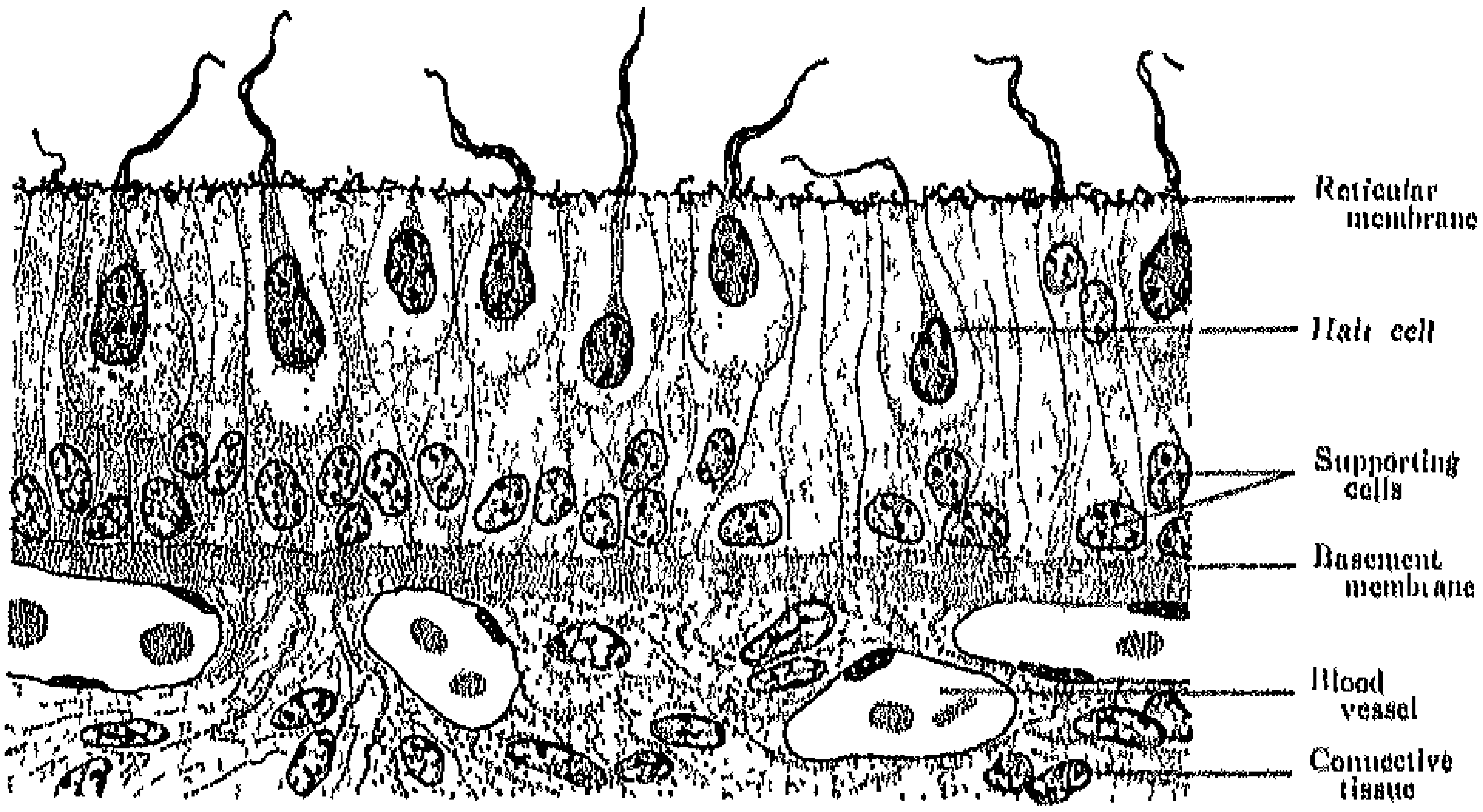


FIG. 285. Detail of macula. Note the deeply staining nuclei of the hair cells and the hairs protruding from the reticular membrane.

portion of the cells. The free surfaces of the cells are provided with cuticular plates which are joined at their edges by thickened, terminal bars. As these cells pass over the border of the maculae they become low columnar, then cuboidal and finally merge with the flattened cells of the general epithelium.

The hair cells are cylindrical shaped cells that lie between the narrow distal portions of the sustentacular cells. The large, spherical, deeply staining nuclei are located in the basal portions of the cells which extend about halfway from the surface to the basement membrane. The free surfaces are provided with cuticular plates which are inserted between those of the sustentacular cells. A single, hairlike process, consisting of many nonmotile cilia which adhere to one another, projects from each hair cell through the cuticular plate and extends across a narrow, endolymph-filled space, to become embedded in the overlying *otolithic membrane.*

The otolithic membrane is a thick, gelatinous structure containing minute, crystalline bodies of calcium carbonate called *otoliths* or *otoconia.* This membrane lies above the epithelium of the maculae and is separated from it by a narrow space containing endolymph.

In the region of the maculae, the connective tissue layer of the

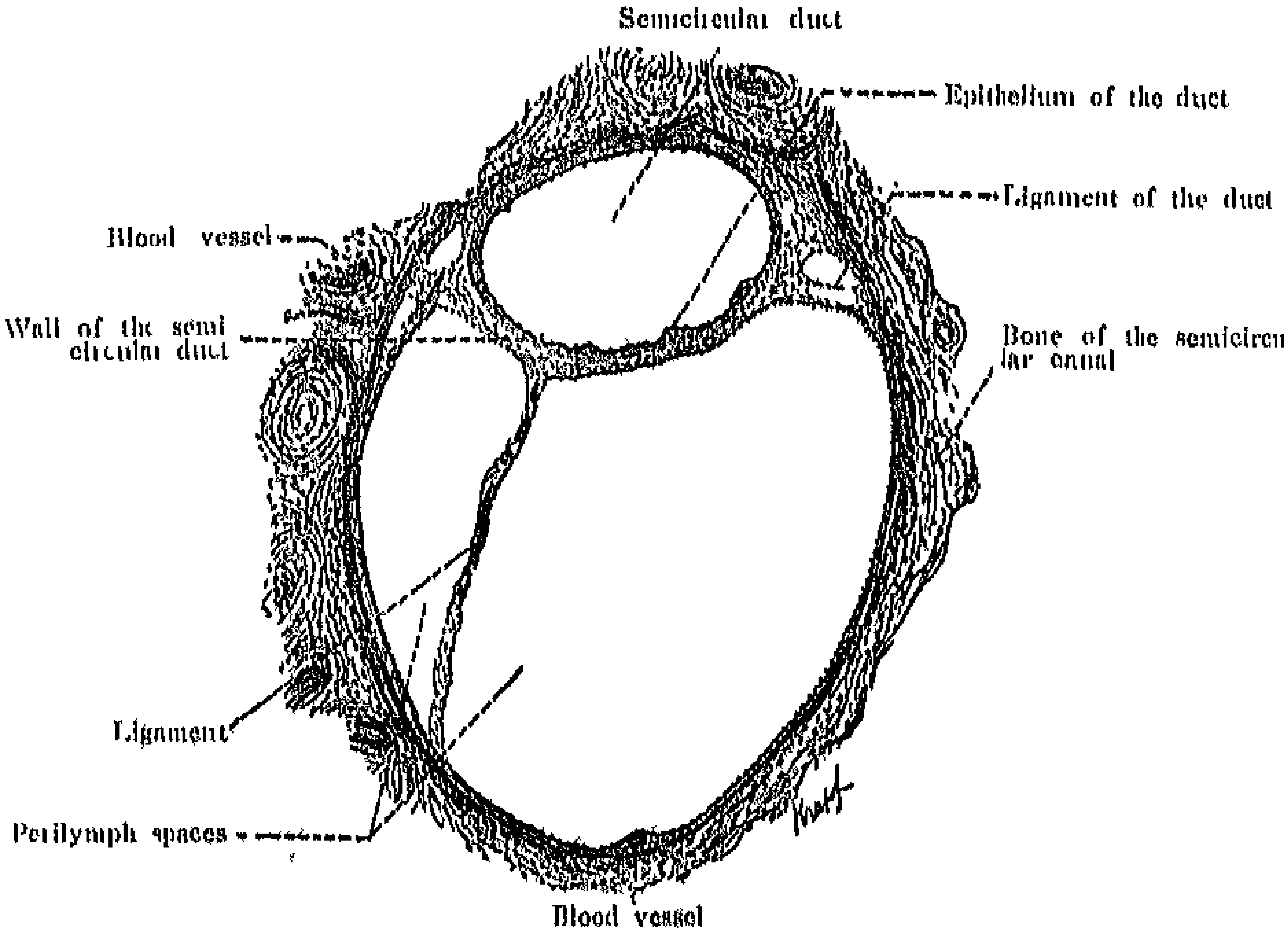


FIG. 286. Cross section of a semicircular duct and the adjacent perilymph spaces together with the semicircular canal of bone in which they are lodged. From a human adult. 50 ×. (Böhm and von Davidoff.) (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

utricle and saccule become greatly thickened. Moreover, in this area the tissue is firmly adherent to the periosteum.

The bodies of the hair cells are surrounded by a fine network of nerve fibers from the vestibular nerve.

The function of the maculae has to do with proprioceptive stimuli relating to equilibrium, particularly with regard to the awareness of the position of the head in space.

The semicircular canals occupy one-third of the bony canals. The membranous canal lies close to the outer wall of the bony canal, the

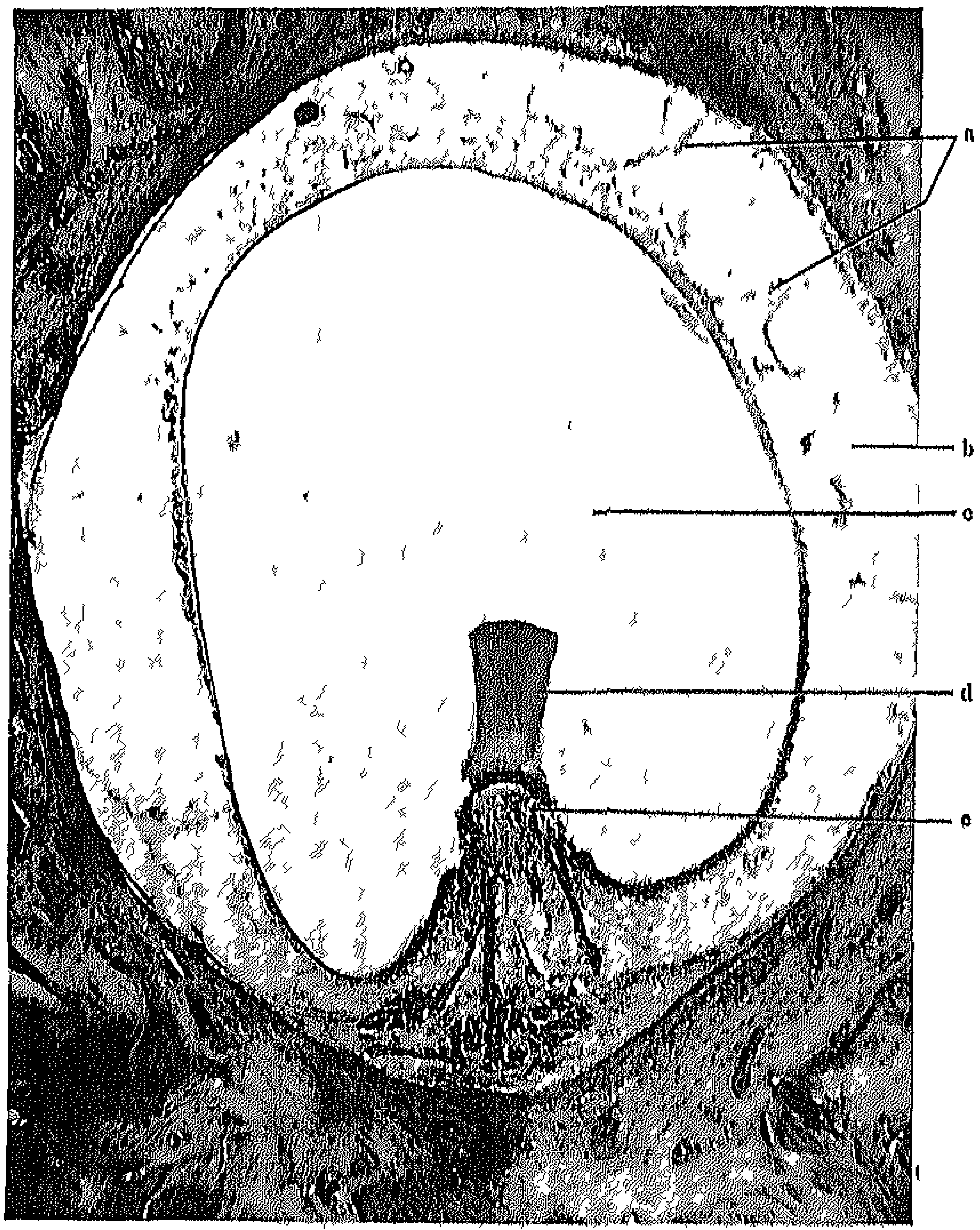


FIG 287. Ampulla of semicircular canal. (a) Trabeculae passing from the periosteal lining of the bony canal to the fibrous portion of the wall of the membranous canal. (b) Perilymph space (c) Endolymph space. (d) Cupula. (e) Crista. Photomicrograph.

connective tissue of its external layer merging with the adjacent periosteum. On the side toward the perilymph space, trabeculae extend from the membranous canal to the wall of the bony canal, thus holding it firmly in place. The side of the membranous canal, which is adjacent to the bone, is convex, the portion of the wall which is toward the perilymph space is slightly concave. Structurally the walls of the membranous canals are similar to those of the utricle and saccule. The epithelium on the convex side is slightly thickened and forms a strip which is know as the *raphe*. The raphe represents the line along which the two lips of the embryonic otic vesicles were fused.

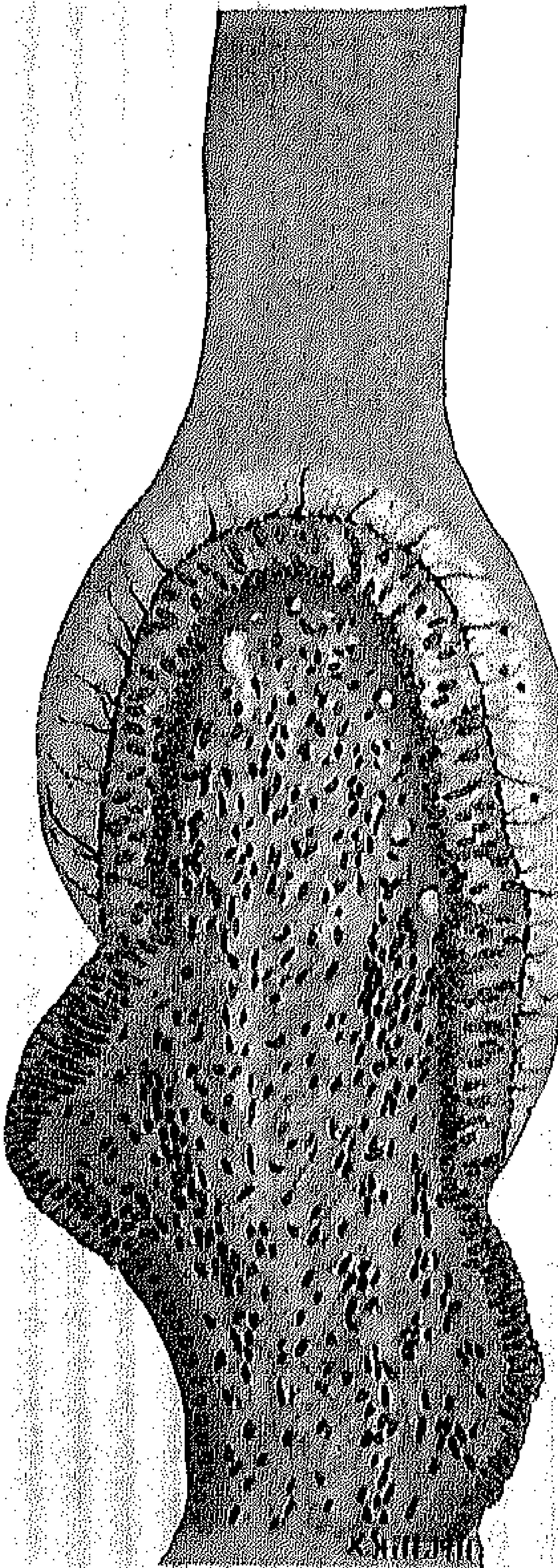
THE CRISTAE. A high moundlike ridge, the *crista ampullaris*, is formed in each ampulla by the thickening and elevation of the subepithelial connective tissue. The epithelium which forms the lining of the ampulla is modified as it passes over the crista and, as in the macula, consists of sustentacular cells and hair cells. In fixed preparations the crista appears to be surmounted by a tall, longitudinally striated structure, the *cupula*. The striated appearance of the cupula is due to the presence of minute canals which are filled with endolymph. The processes of the hair cells, after crossing the narrow endolymph space between the epithelium and the cupula, are lodged in these canals. The processes of the hair cells of the crista are longer and more slender than in the maculae, those springing from the border of the crista bend upward and inward toward the midline of its summit.

It is generally believed that the cupula as seen in fixed preparations is an artefact. In life the hairs extend into a thin gelatinous fluid which fills the ampulla. The cupula is formed by the coagulation of the gelatinous material about the hairs by the reagents employed in preparing the tissue.

The cristae ampullares are the receptive organs concerned with the general sense of equilibrium.

Both the maculae and cristae are supplied by a branch from the vestibular division of the auditory nerve. The fibers of the nerve come into association with the cells of the *vestibular ganglion* in the internal auditory meatus. The fibers of the ganglion cells pass through canals in the bone and are continued in the subepithelial tissue to the basement membranes of the maculae and cristae. Losing their myelin sheaths as they pierce the basement membrane the nerve fibers break up into a number of delicate fibrils which form close pericellular networks about the hair cells.

THE COCHLEAR DUCT. The cochlear duct is the part of the membranous labyrinth that is located in the bony cochlea. It begins as a blind sac *(caecum vestibulare)* in the basal portion of the cochlea, between the oval and round windows. It makes two and one-half turns about the modiolus and ends blindly as the *caecum cupulare* in the



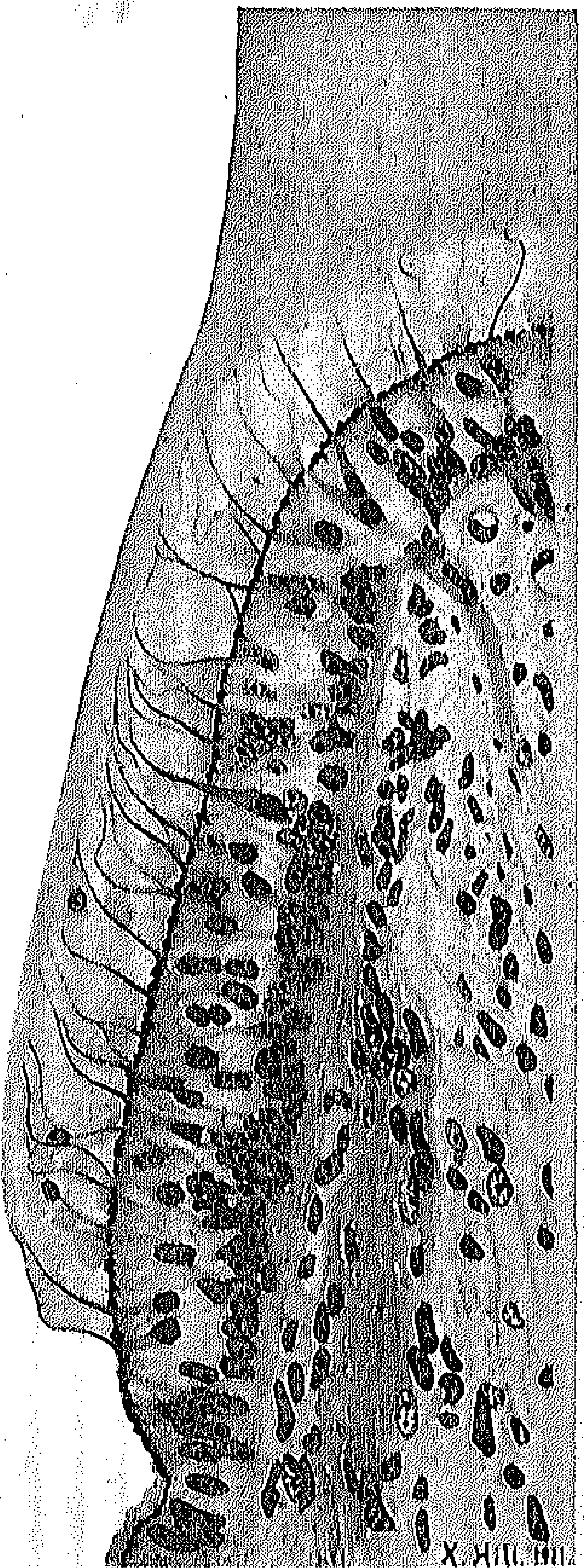


FIG. 288. *(Left)* Crista ampullaris, horizontal canal showing the collar or ridge below the area occupied by neuroepithelium and the more extensive area of hair cells on one side of crista. (Courtesy, Cowdry: "Special Cytology," New York, Paul B. Hoeber, Inc.)

FIG. 289. *(Right)* Preparation showing one-half of crista. Note the long hairs passing from the reticular membrane cross the open space to the under surface of the cupula. (Courtesy, Cowdry: "Special Cytology," New York, Paul B. Hoeber, Inc.)

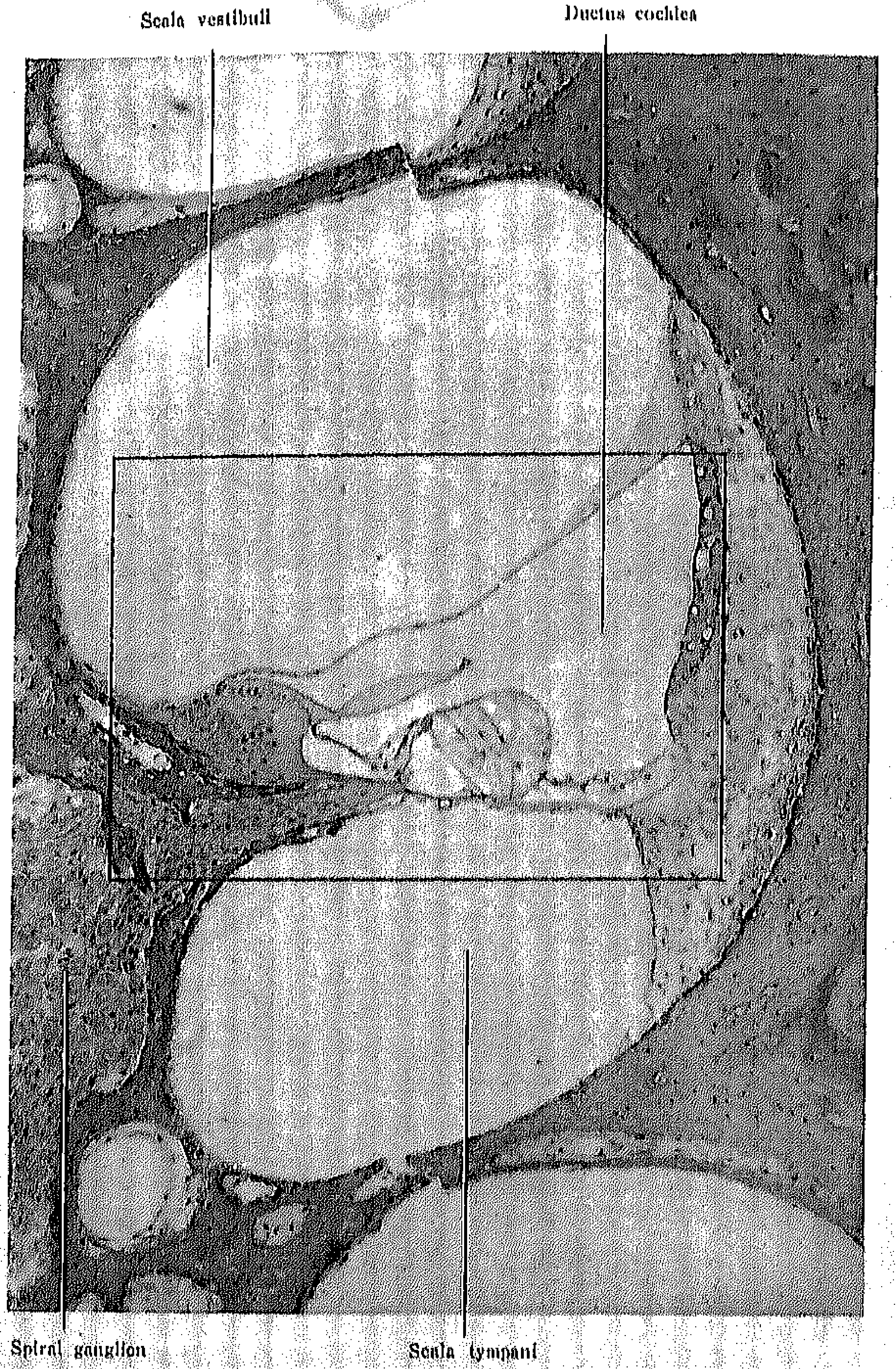


Fig. 290. Axial section of human cochlea. (From the collection of Dr. Dean M. Lierle.) Photomicrograph.

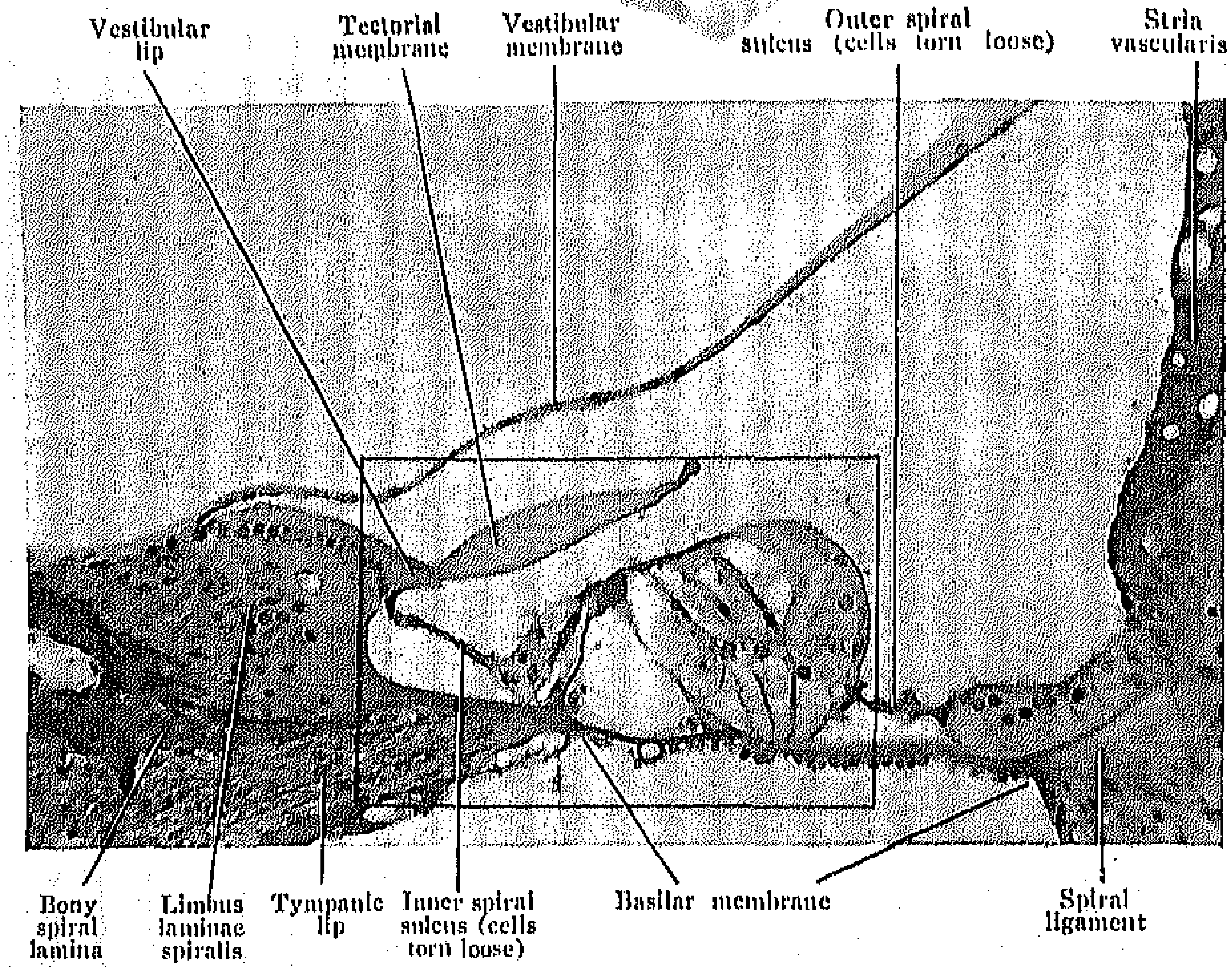


FIG. 291. Section of human cochlea. (From the collection of Dr. Dean M. Lierle.) *Photomicrograph.*

apex or cupula. It is separated from the scala vestibuli by the thin membrane which forms its roof (Reissner's membrane). Its floor is formed by the basilar membrane which separates it from the scala tympani. Both the scala vestibuli and the scala tympani contain perilymph. They communicate through a small aperture, the *helicotrema,* located at the apex of the cochlea. The perilymph spaces are lined by a delicate endosteum and a thin stratum of endosteal tissue, which is covered by a layer of flattened mesothelial cells.

When viewed in section, the cochlear duct appears as a triangular space, the outer wall of which is formed by the spiral ligament, the roof by the membrane of Reissner, and the floor by the basilar membrane.

The spiral ligament consists of a thickening of the endosteal tissue, the fibers of which are densely compacted close to the bony wall of the duct. The fibers which form the part of the ligament that immediately borders the endolymph space are more loosely arranged. The spiral ligament begins on the lateral wall of the cochlear canal a short distance above the attachment of Reissner's membrane and extends a short distance below the level of the basilar membrane, thus forming a part of the outer wall of both the scala vestibuli and the scala tympani.

The outer extremity of the basilar membrane is attached to the

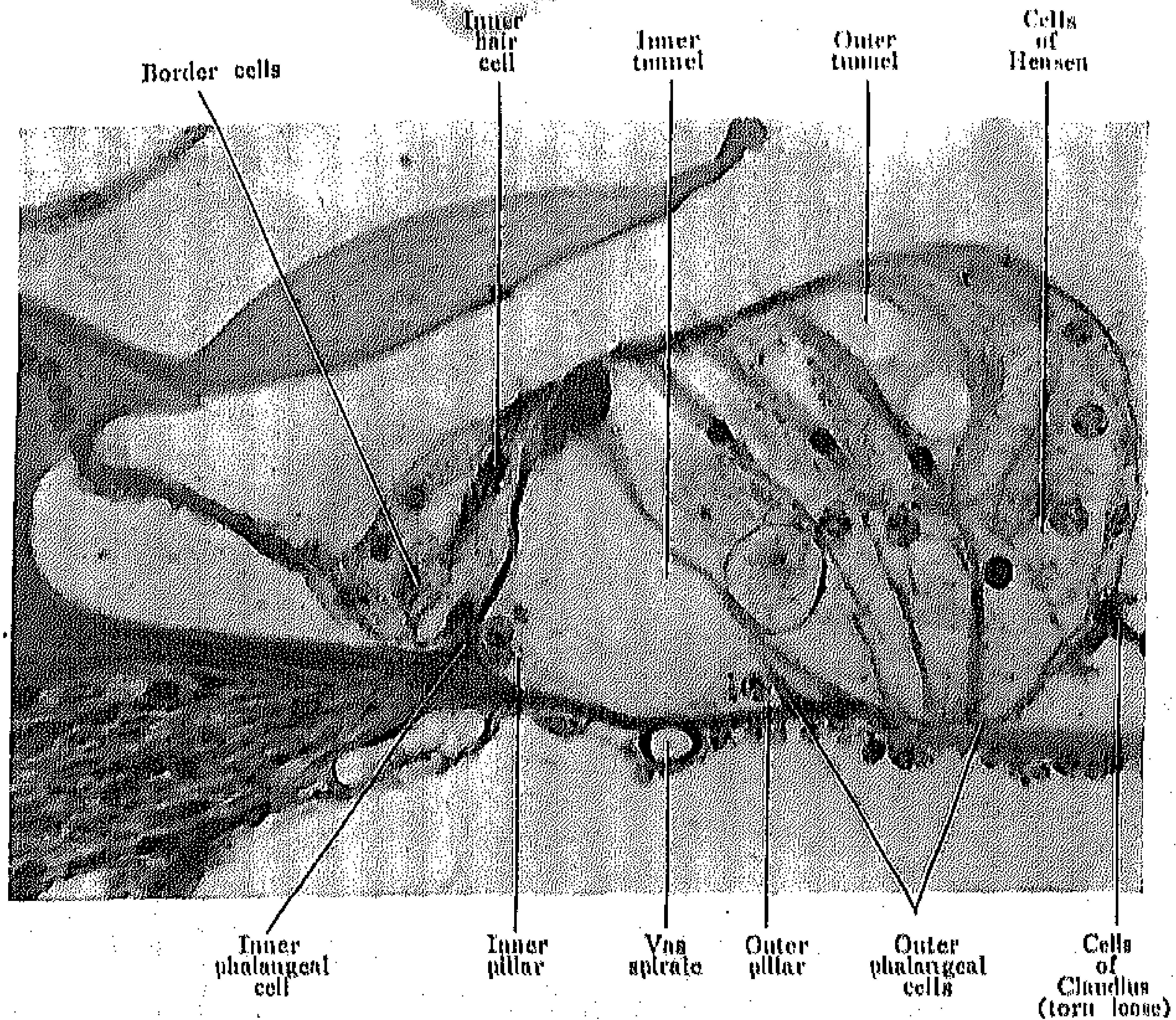


FIG. 292. Section of human organ of Corti. (From the collection of Dr. Dean M. Lierle.) Photomicrograph.

crista basilaris, a thickened projection of the spiral ligament which is triangular in section. A rounded elevation of the spiral ligament a short distance above the crista is called the *spiral prominence.* The shallow groove between the spiral prominence and the crista basilaris is known as the *external spiral sulcus.* Both the spiral prominence and the external spiral sulcus are covered by a layer of simple cuboidal cells. The crista basilaris, the spiral prominence and the external spiral sulcus follow the spiral turns of the cochlear duct from the base of the cochlear canal to its apex.

Above the spiral prominence the epithelium which forms the lining of the cochlear duct is a low pseudostratified or stratified columnar type. The loosely arranged subepithelial connective tissue contains numerous blood vessels, due to which this portion of the spiral ligament is known as the *stria vascularis.* It is believed that the endolymph which is known to undergo change and renewal in the cochlear duct is secreted through the stria vascularis. Shambaugh, however, reports the finding of a true endolymph secreting apparatus in the epithelium of the sulcus externis. He suggests that probably the stria functions as a mechanism for regulating the pressure of the endolymph.

Reissner's membrane which forms the vestibular wall or "roof" of the cochlear duct, although it is an extremely thin structure, consists of three layers: a substantia propria which is composed of a network of delicate connective tissue fibers, a thin layer of mesothelial cells covering its vestibular surface, and a layer of flattened epithelial cells which lie upon its cochlear surface. In the lower animals the fibers of the substantia propria support a network of small capillary vessels, but in man the membrane is said to be avascular. The mesothelial cells which form the outer covering of the membrane are continuous with the mesothelium that forms the lining of the scala vestibuli. The flattened squamous cells on its cochlear surface are ectodermal in origin and are continuous with the epithelial lining of the cochlear duct. Reissner's membrane is attached to the spiral ligament a short distance below its vestibular border. It passes obliquely, at a sharp angle, downward and inward and ends in being attached to the base of the vestibular lip of the spiral limbus.

The use of the terms "upper" and "lower," "inner" and "outer" as applied to the cochlea, assumes that the long axis of the modiolus is vertical in direction. As a matter of fact, the base of the modiolus is medial in direction, its apex pointing laterally, the direction of its long axis being mediolateral. The assumption of a vertical direction for the long axis of the modiolus is for the purpose of simplifying description.

The *spiral limbus* is formed by a thickening of the periosteal tissue at the base of the bony spiral lamina. It consists of two limbs, usually spoken of as the upper or *vestibular lip* and the lower or *tympanic lip*. The deep groove between the vestibular and tympanic lips is called the *internal spiral sulcus*. The upper surface of the vestibular lip is marked by a series of radially directed grooves and ridges. The ridges extend slightly beyond the free border of the lip, forming a number of toothlike projections, the *auditory teeth of Huschka*.

The epithelium by which its surface is covered consists of flattened, polygonal cells over the ridges and low columnar cells in the grooves. The epithelium which forms the lining of the internal spiral sulcus is cuboidal, the cells becoming flattened as they extend laterally on the cochlear surface of the tympanic lip. The tympanic lip of the spiral limbus just before it joins the basilar membrane is perforated by numerous apertures for the passage of the fibers of the cochlear branch of the auditory nerve. These apertures are known as the *foramina nervosa*.

The *basilar membrane (membranous spiral ligament)* extends from the outer border of the tympanic lip of the spiral limbus to the crista

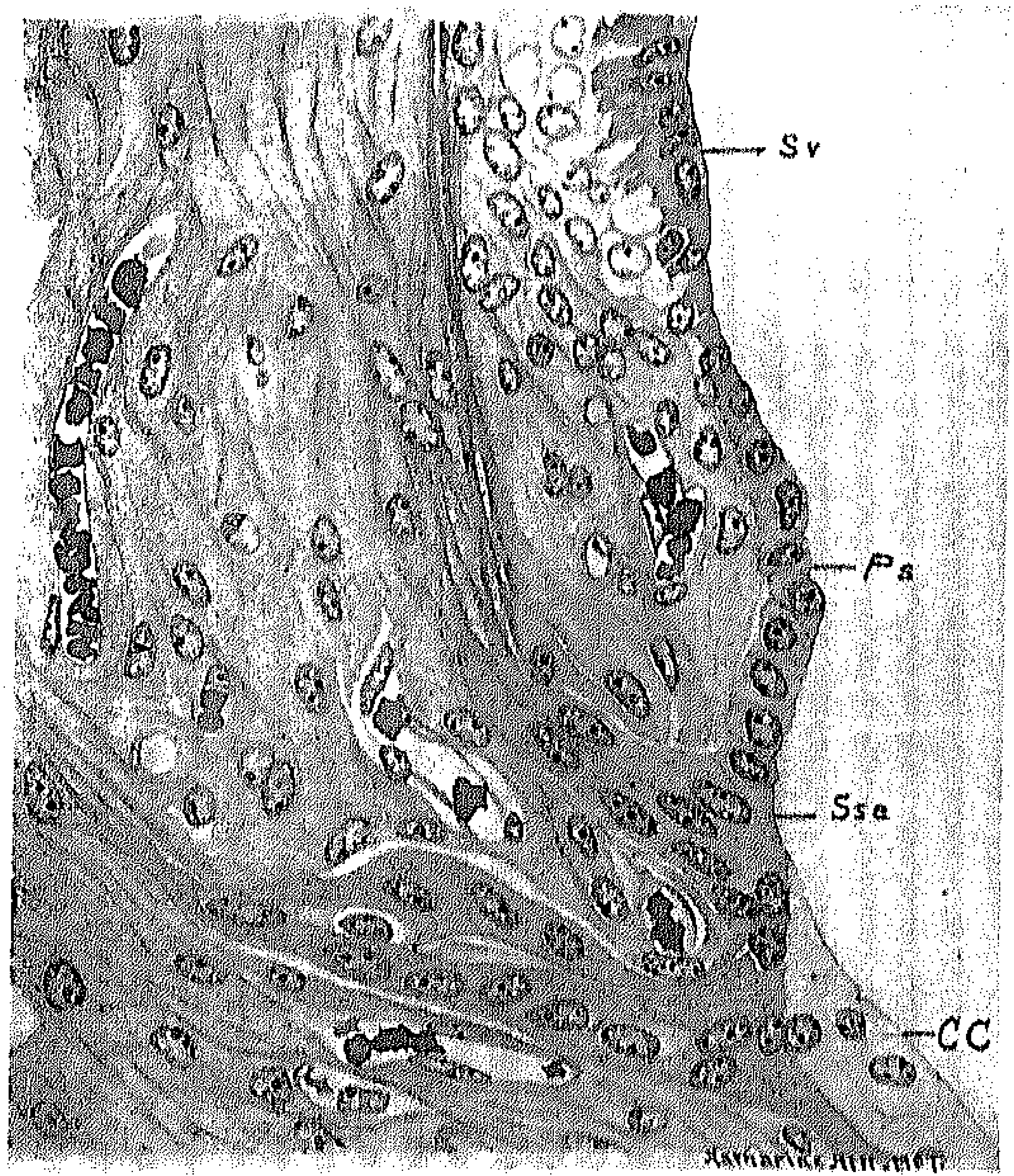


Fig. 293. Section of outer wall of ductus cochlearis showing from above downward. (Sv) Stria vascularis. (Ps) Prominentia spiralis. (Ssc) Sulcus spiralis externus. (Cc) Cells of Claudius. (Courtesy, Cowdry: "Special Cytology," New York, Paul B. Hoeber, Inc.)

basilaris of the spiral ligament. As the bony spiral lamina extends beyond the outer border of the tympanic lip, the inner portion of the basilar membrane rests upon it. The membrane is divided into an inner portion, the *zona arcuata*, extending from the medial side of the inner pillar to the outer pillar of Corti, and an inner portion, the *zona pectinata*, which continues from the outer pillar of Corti to the apex of the crista basilaris. It consists of three layers: a *substantia propria*, usually referred to as the *middle fibrous layer*, the *tympanic layer* and an *epithelial layer*.

The *middle fibrous layer* consists of delicate connective tissue fibers which, continuing into the membrane from the spiral limbus, form a delicate network in the zona arcuata. In addition to a small amount of supporting tissue, the zona pectinata contains a number of large, highly refractive, nonbranching fibers which pass radially from the feet of the outer pillars of Corti to the crista basilaris in which they become dispersed among the fibers of the spiral ligament. These fibers which are known as the *auditory strings*, increase in length from the base of the cochlea to its apex. This increase in the length of the auditory strings corresponds to a similar increase in the width of the basilar membrane.

The *tympanic covering layer* consists of loosely arranged fibrous tissue on the tympanic surface of the basilar membrane. Besides its loosely arranged fibers, it contains a number of spindle-shaped connective tissue cells. However, there is no definitely formed mesothelial layer covering its surface. The portion of the layer which belongs to the zona arcuata contains numerous blood vessels. These vessels empty into a large vein located immediately below the tunnel of Corti and known as the *vas spirale*. Blood vessels are not present in the layer belonging to the zona pectinata. A nearly homogeneous layer containing a few fibers and nuclei, is located between the substantia propria and the epithelium. This is known as the *vestibular covering layer*.

The *epithelial* or *cochlear layer* of the basilar membrane forms a thickened ridge, the cells of which are modified to form a highly complex, neuroepithelial structure, the *organ of Corti*. This ridge follows a spiral course from the caecum vestibulare at the base of the cochlea to the caecum cupulare at its apex. The organ of Corti is the structure concerned with hearing.

THE ORGAN OF CORTI. The basilar membrane supports the neuroepithelial structure of the cochlear duct, the organ of Corti. This structure, like the maculae and cristae, consists of two types of cells: supporting or sustentacular cells and hair cells. The real neuroepithelial cells are the hair cells which are in relation to the fibers of the cochlear nerve. A number of specialized cells make up the organ of Corti and in order, beginning at the inner side they are: *border cells, inner hair cells, inner phalangeal cells, inner pillar cells, outer pillar cells, outer phalangeal cells (Deiters' cells), outer hair cells* and *cells of Hensen.*

The inner side of the organ of Corti is supported by a single row of tall, slender cells, the *border cells,* which extend from the basilar membrane to the surface of the epithelium. Their free edges are provided with cuticular plates.

The *inner hair cells,* forming a single row on the outer side of the border cells, are short cylindrical elements which extend from the surface to about one-half the depth of the epithelial layer. Their rounded basal portions in which their spherical nuclei are located, are supported by the border cells and the expanded portions of the inner phalangeal cells. Their cytoplasm is filled with fine granules. The

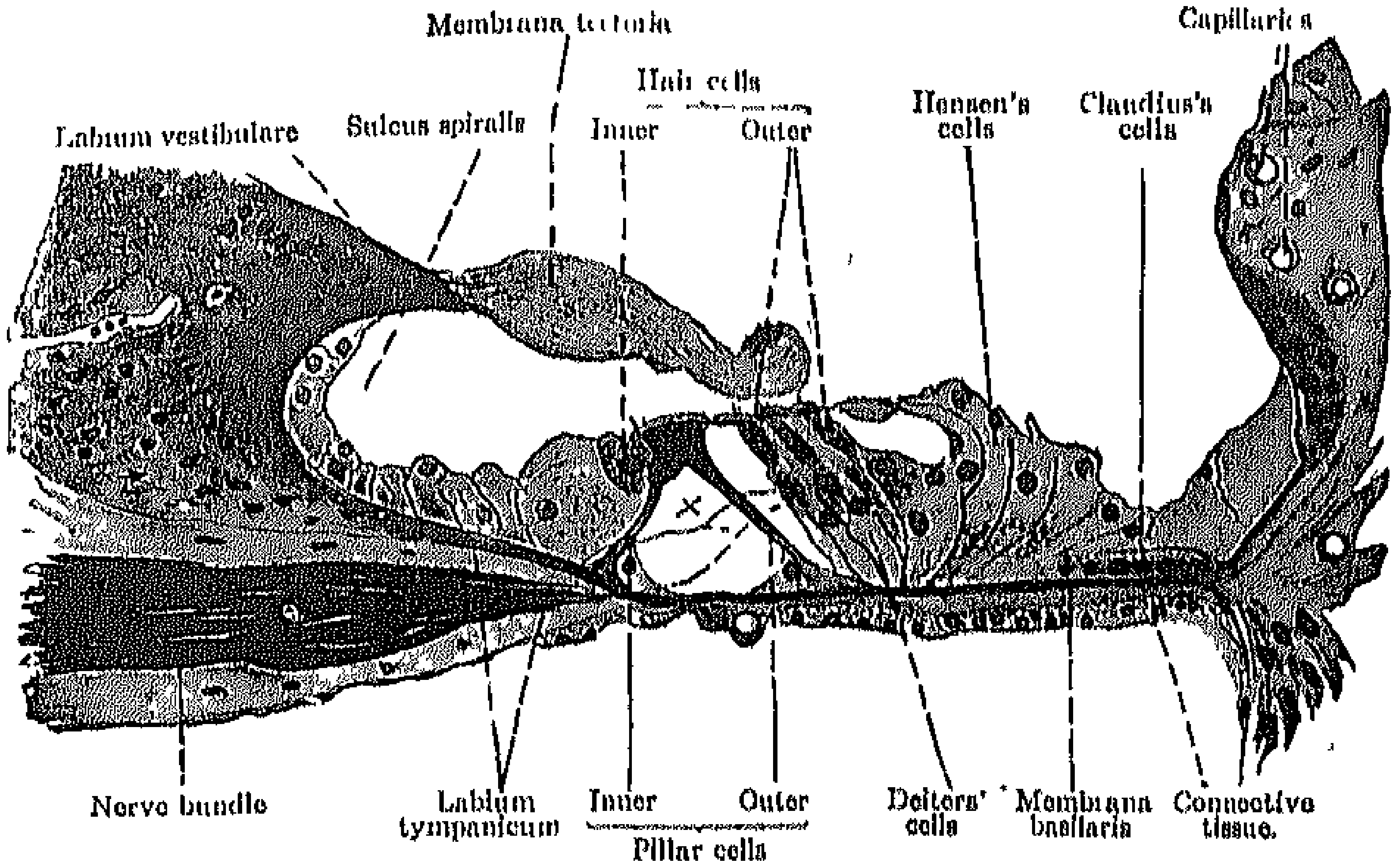


Fig. 291. Organ of Corti. 210 ×. (X) Intercellular "tunnel" transversed by nerve fibers. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

surfaces of the hair cells are provided with cuticular plates through which stiff, hairlike processes project into the cochlear duct.

The *inner phalangeal cells* form a single row of slender cellular elements which are located between the inner hair cells and the inner pillar of Corti. They are tall cylindrical cells, having an expanded proximal portion that rests on the basilar membrane, and a narrow distal portion, the *phalangeal process*, extending to the surface of the epithelium. The free ends of the phalangeal processes bear cuticular plates which articulate with the cuticular plates of the border cells and hair cells, an arrangement that provides a strong support for the hair cells.

External to the structures described above are two sets of rodlike structures, the *inner* and *outer pillars of Corti.* Each pillar consists of a bundle of stiff fibrils *(tonofibrils)* which are deeply stained in preparations. The ends of the pillars, which rest on the basilar membrane, are expanded and form the feet while their expanded distal ends are known as the heads. The convex surfaces of the heads of the outer pillars fit into corresponding concavities in the heads of the inner pillars, forming an articulation which bears a close resemblance to a ball-and-socket joint. The pillars diverge as they extend toward the basilar membrane, enclosing between them a triangular space containing endolymph and known as the *tunnel of Corti.* The rodlike bundles of tonofibrils are enveloped by a thin layer of protoplasm

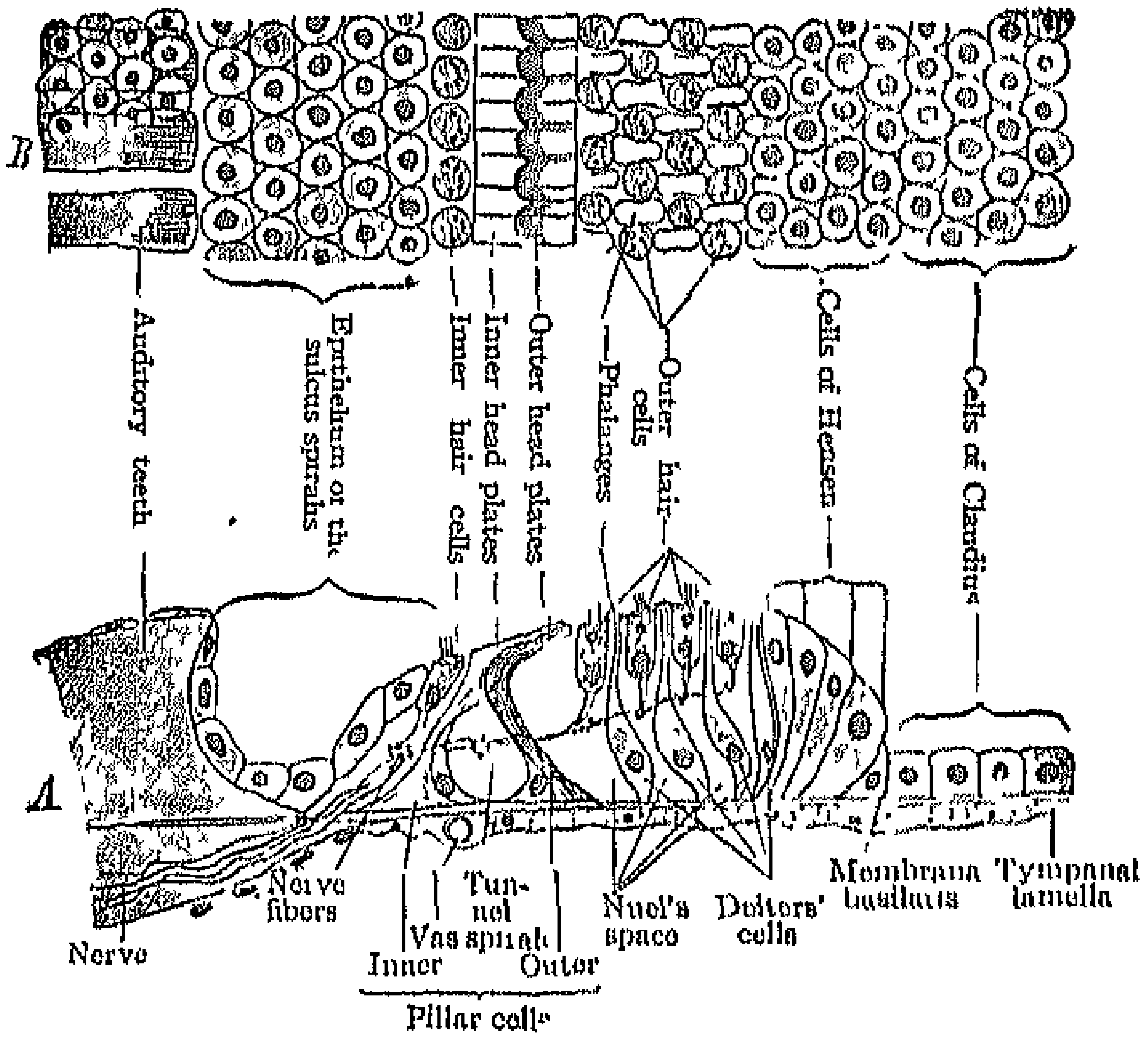


FIG. 295. Diagram of the structure of the basal wall of the duct of the cochlea. (A) View from the side. (B) View from the surface. In the latter the free surface is in focus. It is evident that the epithelium of the sulcus spiralis, lying in another plane, as well as the cells of Claudius, can be seen distinctly only by lowering the tube. The membrana tectoria is not drawn. The spiral nerves are indicated by dots. (Courtesy, Bremer-Weatherford: "Textbook of Histology," Philadelphia, The Blakiston Company.)

which extends upward from the pillar cell. Each pillar cell consists of a mass of protoplasm located on the tunnel side of the foot of each pillar and contains a large spherical nucleus. The heads of the pillars bear on their free surfaces large cuticular plates to which the rods, formed of tonofibrils, are attached. The cuticular plates of the outer pillars extend outward and articulate with the cuticular *(phalangeal)* plates of the cells of Deiters. The cuticular plates of the inner pillars lie upon the plates of the outer pillars but do not extend quite to their borders. The number of outer pillar cells has been estimated to be 3850, the number of the inner pillar cells at 5600. Owing to this difference in the number of outer and inner pillar cells, the head of a single outer pillar may articulate with two, or even three pillar cells.

Two kinds of cells are located immediately external to the outer pillar cells: the *outer phalangeal cells (cells of Deiters)* and the *outer hair cells.*

The *outer phalangeal cells* have a broad proximal portion which rests on the basilar membrane, and a narrow, slender distal portion, the *phalangeal process,* which extends to the surface where it becomes expanded and bears a broad cuticular plate. The nuclei of the outer phalangeal cells are located in their proximal part. The cytoplasm is granular. These cells are supported by small, deeply staining bundles of tonofibrils. Each bundle consists of two parts, one of which forms a supporting structure beneath the hair cells with which the outer phalangeal cells alternate, and the other extends to the surface in the phalangeal process and is attached to the cuticular plate. The outer phalangeal cells are arranged so that the cuticular plates borne on the surface of their phalangeal processes, fit together and form an alternating series, between which are the openings occupied by the cuticular plates of the hair cells. This structure, formed by the interarticulating cuticular plates of the outer phalangeal cells and the hair cells, is called the *reticular membrane*.

The inner row of the outer phalangeal cells is located so that a considerable space, known as the *space of Nuel,* is formed between them and the outer pillars of Corti. This space follows the spiral turns of the cochlear duct and forms a canal, the *canal of Nuel,* which parallels the tunnel of Corti. Both of these canals are filled with a semigelatinous substance which gives support to the nerve fibers passing through them.

The *outer hair cells,* of which there are three to five rows depending on the location, are broad columnar elements located in the upper one-third of the organ of Corti. Their spherical nuclei are located in their rounded basal portions which rests on the broad proximal portion of the outer phalangeal cells.

The *cells of Hensen* which are located external to the outer pharyngeal cells give additional support to the organ of Corti at the outer border. They are tall columnar cells with slender proximal portions and enlarged distal portions in which their spherical nuclei are located. The cells of Hensen are arranged in three or four rows, the cells of each row becoming shorter until they are merged with the cells of Claudius.

The *cells of Claudius* are cuboidal cells which form the epithelium of the outer portion of the basilar membrane. This epithelium is continued as the lining of the external spiral sulcus. The cells of Claudius are characterized by their small nuclei and clear nongranular cytoplasm. In the basal coil of the cochlear duct, groups of small cells having a deeply staining cytoplasm, lie between the cells of Claudius and the basilar membrane. These cells are known as the *cells of Boettcher.*

The tectorial membrane is a cuticular structure having a striated appearance. It extends from the vestibular lip of the spiral limbus to a little beyond the outer row of hair cells, its position being just above

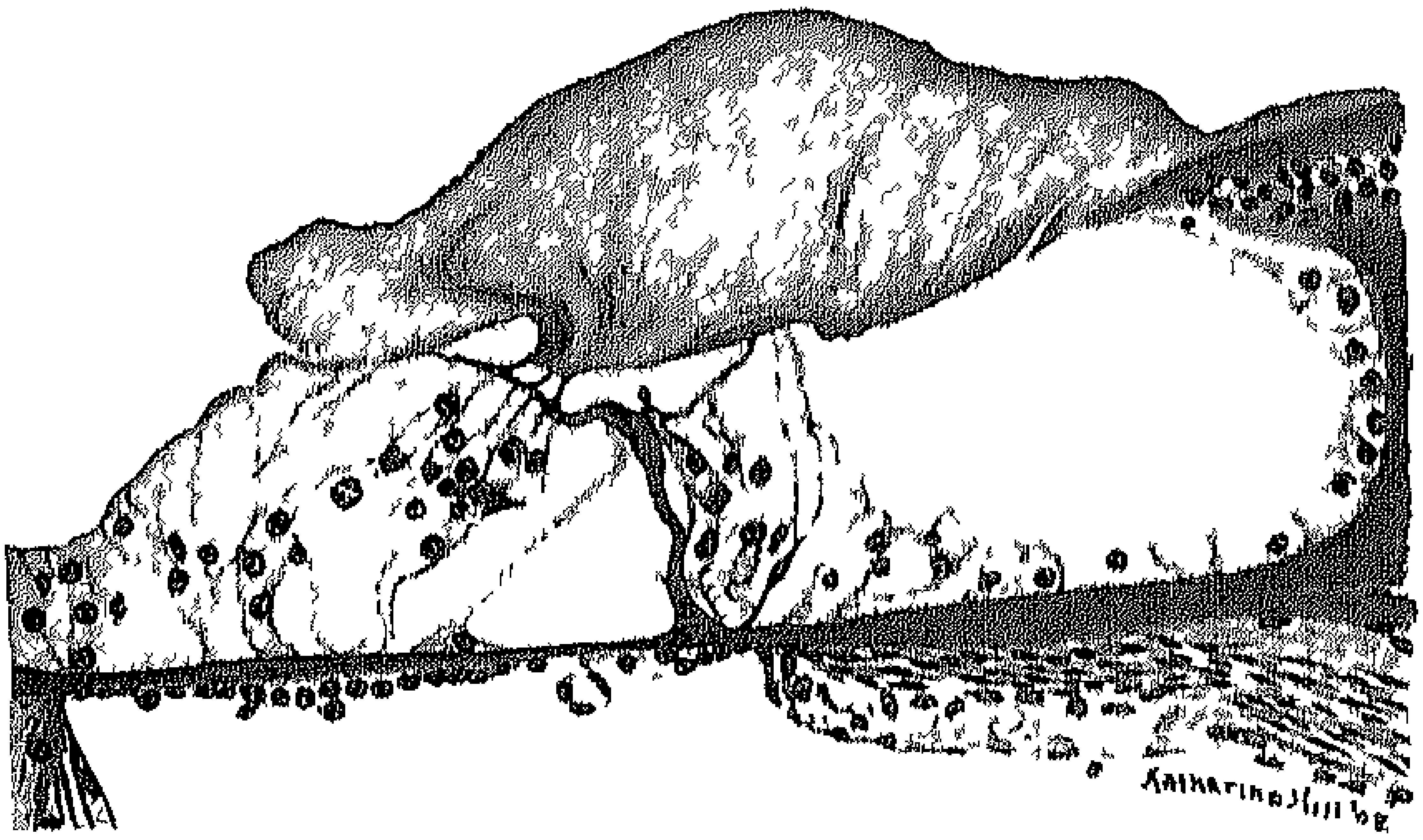


FIG. 296 Papilla spiralis showing attachment of hairs of the outer cells to membrana tectoria, also attachment of stripe of Hensen to the inner border cells which have been drawn out as the result of contraction of the tectorial membrane (Courtesy, Cowdry: "Special Cytology," New York, Paul B. Hoeber, Inc.)

the organ of Corti. The tectorial membrane consists of fibers which radiate from the outer border of the vestibular lip of the limbus to the margin of the membrane. The fibers which give it its striated appearance are bound together by a homogeneous interfibrillar substance. The upper surface of the membrane is curved convexly, the lower surface being correspondingly concave except in the middle portion which is somewhat thickened. A nonstriated, dark band on the under surface of the membrane is known as the *stripe of Hensen.* Corresponding to the increase in the width of the basilar membrane, the width of the tectorial membrane increases from the base of the cochlea to its apex.

The fibers of the *cochlear division of the auditory nerve* enter the modiolus at its base and continue in the central canal to its apex. In its course the nerve gives off bundles of fibers which pass to the spiral canal at the base of the bony spiral lamina where they are in association with the *bipolar cells* of the *spinal ganglion.* Fibers from the ganglion cells are continued in a canal between the upper and lower plates of the bony spiral lamina, from which they enter the subepithelial connective tissue of the tympanic lip of the limbus. Passing through the foramina nervosa, the fibers lose their myelin sheaths and form two bundles, one of which passes to the inner hair cells, the other continuing between the pillars of Corti and crossing the tunnel of Corti and the space of Nuel ends in relation to the outer hair cells. The fibers of both bundles end in pericellular networks about both the inner and outer rows of hair cells.

ACTION OF THE AUDITORY APPARATUS

For a detailed discussion of function of the mechanism of the ear, the student should refer to a good textbook of physiology. Briefly, however, it consists essentially of the following sequence of events.

Sound waves striking against the tympanic membrane start it to vibrating. These vibrations are transmitted by the ossicles to the perilymph in the scala vestibuli of the inner ear, where pressure waves are produced. This perilymph is enclosed in a space formed by bone and the thin membrane of Reissner throughout the length of the cochlea. At the apex of the cochlea, however, it communicates through a small opening, the helicotrema with the perilymph of the scala tympani. The scala tympani, like the scala vestibuli, is bounded by bone and the fairly rigid basilar membrane. At the base of the cochlea the perilymph is confined within the scala tympani by the membranous secondary tympanic membrane which closes the round window. Thus there are two possible pathways for transmission of pressure waves set up in the perilymph of the scala vestibuli. They might be transmitted by way of the helicotrema to the perilymph of the scala tympani and be "damped off" by way of the secondary tympanic membrane (occurs when sound is very great and very strong pressure waves are produced) or the pressure waves could be transmitted across Reissner's membrane to the endolymph of the cochlear duct. Vibrations of the endolymph may act on both the tectorial membrane and the basilar membrane starting them to vibrating. It is a question which of these two structures is affected most, whether the hair cells on the basilar membrane are brought up against the tectorial membrane or whether the tectorial membrane is forced down against the hair cells. It is possible that both may occur. Apart from that debatable question, the hair cells are stimulated and the pressure waves are transformed into stimuli by the hair cells and carried to the auditory centers in the brain by way of the auditory nerves and there translated into what we recognize as sound. For the discussion concerning the theories of interpretation of pitch and tone, the reader is referred to a text of physiology.

Laboratory Directions

The study of all histological tissues can be reduced to the study of the details of cells, fibers, ground substance or matrix, and their relationships. In such a study, the student should attempt to learn not only the morphology, but also to note any criteria that might indicate functional activity.

In this study of detail, the student *must not* lose sight of the fact that all tissue elements of the body are subject to variation and he should be extremely careful in selecting an area for study. It is necessary to first examine the entire section in order to choose a "typical" area for the study of histological detail. Many beginning students seem to have the faculty of choosing atypical areas for examination. If the section happens to be an organ which is made up of several fundamental tissues, these areas of different tissues should be noted when the section is examined under low power and each area subjected to careful examination later under higher magnification.

If the student studies the fundamental tissues carefully and learns well their characteristics, the understanding and identification of organs becomes a relatively simple procedure, since they are merely these fundamental tissues in definite relationships, together with certain specialized cells which are specific and characteristic for that particular organ.

At this point the student should also be warned of the danger of depending on "color" of sections rather than learning to recognize them by their structural characteristics. Most of the sections used in teaching are stained with hematoxylin and eosin and students may be completely confused if confronted with identical sections stained by any other method, unless they are familiar with morphological characteristics.

A SUGGESTED METHOD OF LABORATORY TEACHING IN HISTOLOGY

The following laboratory procedure has been used and the results were so gratifying, both to the instructors and the students, that it is being suggested as a possible departure from the usual methods.

It is essentially an oral examination method over each assignment. The method is particularly helpful during the first part of the course in histology when the students are learning to "see" and interpret the tissue constituents they are called upon to deal with.

The method may be outlined as follows:

1. The assignment is made and the student studies the necessary sections.

2. When the student feels he is thoroughly familiar with the material he indicates that he is ready to go over the assigned material with the instructor.

3. Using different cuts and slides of the same material (various stains are also helpful in emphasizing morphological characters of the tissue and in discouraging the student from developing the unfortunate habits of depending on color and "grossing" the slides), the instructor asks questions concerning the tissue. The student should be asked to point out (the use of a pointer in the ocular is absolutely essential) certain cells or cellular details and to discuss or explain the significance of various relationships. The use of the pointer prevents any evasion on the part of the student and allows for no misunderstanding between instructor and student. If the student is properly prepared, the period of questioning need not take more than 10 minutes at the most. If he is poorly prepared it is soon evident and he should be sent back to his desk to do the lesson more thoroughly. He should be graded accordingly. If his recitation is satisfactory, he goes on the next assignment.

One major objection which will be raised against the method is the time element involved. This method also demands a great deal of the teaching staff since it utilizes fully their time and energy to the greatest possible advantage for the student.

However, the points in favor of the method, judged by the results, far outweigh these objections. They are:

1. A closer contact and understanding between students and staff members.

2. The student learns immediately the necessity of looking at tissues carefully and critically. He sees details and gains an understanding of the material that, left to himself, he might never be aware of, or at least his appreciation may come so late that he will fail to appreciate and understand many related bits of information in other courses. Judicious and pertinent questions on the part of the instructor can stimulate the interest and curiosity of the student in histology.

3. It is impossible for students to really "loaf along" in the course or to evade the questions. The better students are not held back but can proceed with advanced assignments at their own speed. If it is desirable to keep the class together, the faster students may be allowed to do outside reading for several periods, to allow the slower students to catch up.

4. This method does not allow for any form of cheating. The student soon learns he must rely entirely upon himself and his own information.

5. The student soon learns to understand his material, with the result that he enjoys the work. Identification of unknown slides becomes relatively simple.

6. Time which is usually devoted to making drawings or idling is used for outside reading assignments of pertinent research in the field, which the students, with their understanding of the material, do willingly and enjoy.

7. The student rapidly develops a self-confidence which is gratifying and challenging.

8. He is prepared to enter the course in Pathology with a good, sound foundation and an appreciation of the morphology, relationship, and function of the so-called normal tissues.

9. The grades of the entire class take a marked upward swing, the number flunking is reduced to a minimum and certainly represents those who are inadequate to meet the standards.

STUDY OF A TYPICAL CELL

This study is not intended as an introduction to cytology, but as a review of the cell and its structure. While the following directions apply to the examination of the ova which are to be observed in sections of the ovaries of any of the smaller animals, they apply as well to any cell in which the typical characteristics of cell structure appear.

1. Using the low power, search the section or preparation until a cell is found in which the characteristics of a typical cell as described can be observed.

2. Examine the cell with the high power. Note the cytoplasm. Does it present a homogeneous, a granular or a reticulated appearance? In most egg cells *(ova)* the cytoplasm is obscured by the number of yolk granules *(deutoplasm)* which it contains. Note the cell membrane. In most ova this structure is clearly defined. Observe the nucleus. Note its sharply defined nuclear membrane; the linin fibers—clear, colorless threads forming a delicate network *(neucleoreticulum)*; the small, somewhat amorphous masses of deeply stained chromatin. What is the relation of the chromatin masses to the linin fibers? To the nuclear membrane? In what part of the nucleus are the chromatin masses most abundant? Do they seem to be arranged in a definite pattern? Identify the nucleolus. What is its position in the nucleus? Identify the two types of nucleoli. Does the nucleus contain one or more nucleoli? In specially stained sections observe the Golgi apparatus, and mitochondria. Note their form and position within the cell. What stains were used to stain the Golgi apparatus? What stains mitochondria?

The foregoing study should be continued with the examination of typical cells from the ovaries and spermaries of insects, crayfishes and other forms until the *idea* of the cell and its structure has been firmly established.

Make carefully executed drawings of each type of cell examined.

STUDY OF MITOSIS

MITOSIS IN THE ROOT TIP OF AN ONION. Since direct cell division or *amitosis* is not common in animal tissues, attention will be confined in the following study of cell division to the different stages or phases of *mitosis*. Sections of the growing root tip of an onion stained with Heidenhain's iron-hematoxylin, provide satisfactory material for this study.

1. With the low power examine the sections, of which several may be mounted on a single slide. Note the manner in which the cells are united to form the *tissue* of which the root tip is composed. What is the character of the walls of these cells? Why are walls of this type required in the cells of plants? Note the part of the section in which mitotic figures are most abundant. In what part of the root tip is growth most actively taking place? What is the evidence for this? What is the difference in the appearance of the cells near the tip of the root and of those in the older portions of the section? What does this difference indicate?

2. Using the high power find and study examples of the different stages of mitotic cell division. More accurate observations are possible if the oil-immersion objective is employed.

a. *The Resting Stage.* Note: the cell wall, observing its thickness; the cytoplasm; the nucleus. How is the chromatin distributed in the nuclei of most of the cells in this stage? How many nucleoli are present in a single nucleus? Are the cells nearer the tip of the root, or those in the older parts of the section most extensively vacuolated? What is the explanation?

b. *The Prophase.* Note that the chromatin granules are assembled in the form of a coiled ribbonlike structure—the spireme. Find a spireme which is formed within the nuclear membrane; also one where the nuclear membrane has disappeared. What change is to be noted in the character of the coils?

c. *The Metaphase.* Note: the spindle; the chromosomes, observing their arrangement about the equator of the spindle. The chromosomes are bent into horseshoe-shaped loops which overlap one another. Observe that the head of each loop is directed toward one or the other pole of the spindle.

d. *The Anaphase.* Note the manner in which the chromosomes have been drawn from their former position about the equator in the direction of the poles of the spindle. Observe that the open part of each loop is toward the equator. In some cells a faint line, the *equatorial plate,* may be seen in the equatorial plane. This line indicates the plane in which the new cell wall will be formed which divides the parent into two daughter cells.

c. *The Telophase.* At each pole of the spindle note the deeply stained mass into which the substance of the chromosomes has been fused. The ends of chromosomes, which have not been completely incorporated into this mass, may be identified. In somewhat more advanced stages of the same phase, note that the chromatin mass is enclosed by a nuclear membrane. Look for the reappearance of nucleoli in the nucleus. The division of the parent cell into the daughter cells is completed when a new cell wall has been formed in the region of the equatorial plate.

Draw examples of each stage in mitotic cell division observed in these sections.

MITOSIS IN THE EGG CELLS OF ASCARIS. For the further study of mitosis the egg cells of *Ascaris* provide excellent material. The egg cells of *Arbacia* (sea urchin), *Cerebratulus* (sea worm), and *Cambarus* (crayfish) may also be used to good advantage for completing this study.

While the study of the root tip of the onion is useful for the conception it gives of mitosis in general, the mitotic figures in the egg cells of Ascaris are more nearly like those which will appear in tissues in which cell proliferation is taking place.

1. With the low power examine the egg cells of Ascaris, sectioned and stained with Heidenhain's iron-hematoxylin, to find the areas in which mitotic figures can be best observed.

2. Using the oil-immersion objective, make the following observations:

a. *Mitosis:* Identify the different phases in mitotic cell division, following the outline already given.

b. *The Centrosome:* Note the small, deeply stained body located close to one of the poles of the spindle—the centriole. Occasionally two centrioles may be seen in a single cell, one at each pole of the spindle, in which case the form of the spindle can be more accurately observed. Observe that the centriole is located in a small, spherical mass of colorless (achromatic) protoplasm—the attraction sphere.

c. *The Achromatic Fibers:* Note the delicate fibers radiating in all directions from the attraction sphere—the astral rays; the spindlelike arrangement of similar fibers between the centrosomes. Note how the fibers which form the spindle converge from the region of the equatorial plate toward the centrosomes. The astral rays (polar radiation) and the spindle together form what is called the amphiaster. Note the manner in which the chromosomes are related to the fibers of the spindle.

In what respects is mitosis in the egg cell of Ascaris and in the onion root tip alike? In what respects does mitosis in Ascaris present a different picture? What conclusions can be drawn from these observations regarding mitotic division in the two types of cells?

Draw the different stages in mitosis of egg cells of Ascaris as observed.

STUDY OF EPITHELIAL TISSUES

Since epithelial tissues are composed of cells which are held closely together by a small amount of cement substance, the study of these tissues will involve, simply, the study of cells. The usual classification of epithelial tissues is based on the arrangement and the shape of the cells in the surface layer. Occasionally, their classification is referred to their function, as in "glandular epithelium," but this designation may be considered as being "superimposed" on the usual one which would still class them as simple columnar cells.

Simple Epithelial Tissues

SIMPLE SQUAMOUS EPITHELIUM. The form and appearance of isolated squamous cells can be observed in desquamated cells from the superficial layer of the epithelium lining the mouth.

Examine a preparation of simple squamous cells with high power. Note: the thin, scalelike appearance of the cells; their oval nuclei; the relative size of the nuclei and their location. Note the appearance of the cytoplasm.

Draw several of the cells, showing their characteristic form and appearance.

Mesothelium. Examine a silver-nitrate preparation of mesentery with high power. Note: the form of the cells, which tend to be diamond-shaped; their irregular serrated borders. The dark lines by which the cells are outlined are formed by the precipitation of the silver salt in the fluid, intercellular substance. Can you see the nuclei of the cells? How does the size of the nuclei compare with the size of the cell as a whole?

Draw several of these cells to show their form and arrangement.

Endothelium. By carefully focusing below the level of the mesothelium, the delicate outlines of the endothelial cells forming the walls of the blood capillaries can be distinguished. In all such preparations, some of the capillaries may be seen projecting beyond the boundaries of the tissue, and these present an even better opportunity for observing the form and arrangement of endothelial cells.

Examine an area for endothelium with high power. Notice that as you try to focus on the endothelial walls of the capillaries that certain relatively large, smooth walled spaces are seen throughout the entire tissue. *These are the walls of the fat cells which lie between the two* layers of the peritoneum. Note the shape of these cells. Can you see any of their nuclei? Do these cells come into focus in the same plane as the endothelial cells? What does this indicate concerning the relative positions of these two tissues? Note the shape of the endothelial cells. How does the form of these cells differ from that of mesothelial cells? How do the lines which outline the cells of an endothelium differ from those which outline the cells of a mesothelium?

By shifting the focus from the upper to the lower levels of the tissue, note that as the lens is lowered, the cells of the mesothelium in the upper level disappear, a layer of similar cells appearing as the lower level is approached (if no blood vessel is interposed). How is this to be explained? What is the relation—to be determined by changing the focal levels—of the two layers of mesothelial cells? This observation will be aided by the examination of a piece of freshly obtained mesentery in normal salt solution.

Draw: The observed form and arrangement of the cells of the mesothelium. *Make a similar drawing of the form and arrangement of the cells of an endothelium.*

SIMPLE CUBOIDAL EPITHELIUM. Using the high power, examine the cells which form the epithelial lining of the tubules seen in a cross-section of the apex of a renal pyramid. To what extent is the intercellular cement substance visible? What is the shape of these cells? What is the shape of the nuclei and where are they located in the cell?

Using the low power, find some of the smaller ducts in sections of the salivary glands, the pancreas and the liver. With the high power observe the cells forming the epithelial lining of these ducts, noting their cuboidal form. In a longitudinal cut through one of these small ducts observe the transition from the cuboidal to the columnar type of epithelium in passing from the smaller to the larger ducts. Is this transition abrupt or gradual? Note the staining reaction of the nucleus and the cytoplasm of several of these cells. Are there granules in the cytoplasm?

Make drawings of several typical cells showing the results of the observations outlined above and indicate from which material it is taken.

SIMPLE COLUMNAR EPITHELIUM. Using the high power, examine sections from the gall bladder, intestine and oviduct. Compare the height of the cells with their widths. *Note the shape and location* of the nuclei. Do any of these cells show cuticular plates or striated borders? Do cuticular plates and striated borders always occur together? Do the columnar cells of all three sections show these cellular modifications? If not, in which sections do the columnar cells show these structures? Can you identify terminal bars in relation to these columnar cells? Do the cells of all three sections have terminal bars? Do any of the cells have cilia? In which sections are the cells ciliated? In an area where cilia are present does every cell of the epithelium have cilia?

Compare the epithelium from these three structures and make a table noting the similarities and differences between the cells which you have observed.

VARIATIONS IN SIMPLE COLUMNAR EPITHELIUM

PSEUDOSTRATIFIED COLUMNAR EPITHELIUM. Examine a section of the trachea with low power. Note that the nuclei of the epithelium which forms its lining are not only of different shapes, but that they are also located at different levels. Change to high power and examine the cellular details. Observe the cilia which appear on the free surfaces of the cells. In well-prepared material a row of highly refractive dots may be seen at the bases of the cilia; these are the centrosomelike bodies, called basal granules, which are regarded as having an important relation to ciliary movement.

Since special techniques are necessary for outlining the cell boundaries, examples of pseudostratified epithelia should be drawn as observed. The oval nuclei belong to the tall, narrow columnar cells which extend from the basement membrane to the free surface of the epithelium. The round nuclei are located in cells which rest on the basement membrane and which extend upward for varying distances without reaching the surface.

GOBLET CELLS. Use hematoxylin and eosin stained sections of colon or the small intestine for the study of these cells.

These cells which produce a mucoid secretion are present in large numbers in the intestinal epithelium. They are really simple unicellular glands and because of their peculiar form they are known as goblet cells. They are readily recognized as clear spaces, oval in outline, among the epithelial cells. They are less abundant in the upper portions of the alimentary canal than in the lower portion, where they are so numerous as to almost completely obscure the cells of the usual epithelial type.

Examine a portion of the epithelium of the intestinal canal with the high power. Note the clear, oval spaces scattered throughout the epithelium. These are the mucus containing portions of the goblet cells. The walls of these cells are formed by a thin layer (pellicle) of protoplasm. Note the shape of the deeply staining nucleus which is located in the basal portion of the cell where it is surrounded by a small amount of granular cytoplasm. How do the nuclei of the goblet cells differ from the nuclei of the usual type of epithelial cell?

In the earlier stages of its development, the mucoid material produced by the goblet cells has a strong affinity for the basic dyes. Goblet cells, in this stage, appear in sections as dark blue, pear-shaped bodies scattered among the columnar cells of the epithelium.

Make a careful study of goblet cells in different stages of their development. Draw several goblet cells representing different phases of secretory activity.

GLANDULAR EPITHELIUM. With the low power examine the simple tubular invaginations which are glands in the mucosa of the intestinal wall. Note that the cells of the glandular epithelium are continuous with the epithelium lining the intestinal canal. Observe portions of these glands that have been cut transversely (it is not possible always to orient the tissue so that a true longitudinal cut through the glands is obtained). Change to high power. Observe the character of the cytoplasm of these cells; the form and position of their nuclei. Do the cells in the glands appear to differ from the cells on the surface of the tissue? If such a change occurs, at what point in the gland does it take place? Observe these gland cells as they appear in a cross section of the gland. How does their shape differ from that of the surface cells?

Draw one or two of these glands showing the relation of the glandular epithelium to the epithelium of the intestine. Draw a cross section of one of the glands to show the form, structure and arrangement of the cells.

Examine a section through the base of the tongue or a section of the submaxillary gland with the low power. Identify the presence of two kinds of glandular structures: (1) Those in which the cells of the glandular epithelium possess a densely granular cytoplasm and are arranged about a small opening or lumen. Note the position and shape of the nucleus. (2) Those in which the cytoplasm of the cells is clear and nongranular, the cells being arranged about a somewhat larger lumen. Note the position and shape of nucleus. The cells of the first kind of gland are known as *serous cells,* and they secrete a watery fluid in which the active elements of the secretion are in solution. The cells of the second kind of gland are known as *mucous cells* and they secrete a mucoid substance. Explain the difference in the size of the lumen in the serous and in the mucous type of gland.

Examine several of the serous secreting cells under high power. Observe the striated appearance of the cytoplasm at the base of the cells. What produces this striated effect? Do all epithelial cells show basal striations? Explain their significance.

STRATIFIED EPITHELIAL TISSUES

A stratified epithelium consists of two or more layers of cells. The basal row of cells is quite similar in all stratified epithelia and they consist of cuboidal or low columnar cells. Because of this, in order to identify the type of epithelium which is stratified, it is necessary to observe the shape of the cells of the free or outer layer.

Since the cell boundaries are usually poorly stained or not stained at all, the student must pay particular attention to the shape and position of the nuclei. If the nuclei of the outer layer are round and occupy the center of a mass of cytoplasm the cell is probably cuboidal and the epithelium is transitional epithelium. If the nuclei are oval or elongated with their long axes perpendicular to the basal line and located so that most of the cytoplasm of the cell is above the nucleus, the epithelium is undoubtedly a stratified columnar or a pseudostratified columnar. Surface cells of the squamous type are readily identified. They are flattened cells in which the long axes of both the cells and the nucleus lie parallel to the surface. The nucleus, however, may be absent.

STRATIFIED SQUAMOUS EPITHELIUM. A section through the epithelial layer of the esophagus provides excellent material for this study. Examine this epithelium with the low power. Note: its general appearance; the number of cell layers (strata); its irregular basal line.

Examine an area of the epithelium with the high power. Note: the low columnar or cuboidal cells of the basal row which rest on the subepithelial tissue; the irregularly polyhedral cells which form the succeeding layers; the change which occurs in the shape of these polyhedral cells as they approach the superficial layers of the epithelium. Observe the shape and appearance of the nuclei of the cells which form the basal layers (germinal layers). Can you find any cells showing mitotic figures? In which layer or layers are such cells found? Explain the significance of these mitotic cells. What is the appearance of the cytoplasm of these cells? What changes take place in the appearance of the nuclei and the cytoplasm of the cells as they approach the surface of the epithelium? Observe that the cells of several of the layers above the basal row are separated by narrow spaces. Are these spaces present in living tissues? Explain. Where the cells are separated by these spaces, see if you can demonstrate protoplasmic bridges?

Observe the cells of the more superficial layers. Note that they lie in close relation to one another and that they tend to become fusiform in shape. Explain this change in the form of these cells. Note, also the difference in their staining reaction and the character of their cytoplasm. Explain this change in the appearance of these cells. Observe the scalelike form of the cells of the surface layer. Compare these cells with the squamous cells taken from the mouth. Is there any evidence that these cells are being desquamated?

Draw a small area of the epithelium as seen with the high power, showing the changes which take place in the cells as they pass from the basal layer to the surface.

Compare the epithelium just studied with that covering the tongue, the lip and the palm of the hand.

STRATIFIED COLUMNAR EPITHELIUM. A stratified columnar epithelium differs from the pseudostratified type in having two or more layers of cells in which only the basal layer rests on the basement membrane, while the layer bordering the free surface consists of columnar cells which may or may not be ciliated. Where more than two layers of cells are present, the intermediate layers are made up of polyhedral cells. Stratified columnar epithelium may occur in the trachea alongside pseudostratified columnar epithelium. The former may be recognized by the presence of a continuous basal row of round nuclei. Where else in the body is stratified columnar epithelium found?

TRANSITIONAL EPITHELIUM. Examine a section of the ureter or the urinary bladder with the high power. Note: the number of cell layers present in the epithelium. What is the shape of the cells which form the basal row? Observe the broadly cuboidal form of the cells of the surface layer. Identify the pear-shaped cells (balloon cells) which lie immediately beneath the surface layer. Observe how the deep surfaces of the cells of the surface layer are indented to fit over the broad, rounded apical portions of the balloon cells. Note the shape and size of the cells of the intermediate layers. Note the soft, granular character of the cytoplasm of which all of the cells are composed. What is the shape and character of the nuclei of these cells? Do these cells rest on a basement membrane?

Compare the epithelium lining the ureter with that lining the urinary bladder.

When an organ lined with transitional epithelium is distended, the superficial cells are drawn out and flattened, the tissue bearing a close resemblance to a thin stratified squamous epithelium. However, transitional epithelium lacks the papillated basal line which is characteristic of stratified squamous epithelium, a fact which aids in distinguishing one from the other.

Make a drawing to show the appearance and structure of transitional epithelium.

METHOD OF IDENTIFICATION OF EPITHELIAL TISSUES

Having studied the details of the structure of epithelial tissues, we are now ready to consider the method for organizing this information for the identification of tissue as presented on practical examination.

The simplest method is by elimination, and with practice a student can become very efficient and accurate in the identification of tissues. The method is as follows:

UNKNOWN SLIDE—TO IDENTIFY TYPE OF EPITHELIUM. Examine the unknown slide grossly to see if it is a solid block or a tubular structure. Next examine the section under low power and locate the epithelial tissue—you know it is a surface layer so look along the edges of the section if it is a solid block of tissue or, if it is a tubular structure, look at the tissue lining the lumen.

Having located the epithelium, the first thing to note is whether it is a simple or a stratified arrangement of cells.

If it is a single layer (simple) of cells then observe the shape of the cells. If the cells are square with round, centrally located nuclei it must be a simple cuboidal epithelium, etc.

Note: Usually the tissue used for the identification of mesothelium and endothelium is a piece of mesentery where the cells are seen in surface view rather than in profile. Both mesothelial and endothelial cells are characterized by their irregular diamond shapes and their serrated borders. If blood vessels are not present in the section endothelium cannot possibly be present.

If the epithelium is stratified look at the surface cells and note their shape. If they are very flattened along an axis parallel to the surface it is probably stratified squamous epithelium (however, it might be transitional epithelium from a distended bladder). Next note the number of cell layers, if there are more than 8 layers it must be stratified squamous. However, look for a papillated basal line, it should be present.

Note: Some students confuse a folded epithelium such as is usually seen in the ureter, with a papillated epithelium. This is a foolish mistake. In such a folded epithelium the free and attached surfaces of the epithelium run parallel to one another, if one surface shows an indentation the other will also. In a papillated epithelium on the other hand, the free surface is more or less straight, while the basal surface is irregularly indented.

If the surface cells are large and rather square with the nuclei well separated and more or less round in shape, indicating that the cells are relatively cuboidal, the epithelium is transitional. The cell layers should be from 4–6 layers thick (the nuclei should be counted in a straight line toward the surface in order to avoid counting two adjacent cells of the same layer).

If the surface cells are columnar it may be either a stratified columnar or a pseudostratified columnar epithelium. Look at the basal row of nuclei. If there is a continuous row of round nuclei and the epithelium is relatively thick it may be called a stratified columnar epithelium.

If the epithelium is not very thick (a pseudostratified columnar can only be as thick as its tallest cell since every cell must reach the basement membrane) and there are round nuclei intermixed with elongated nuclei of tall columnar cells in the basal row, it is a pseudostratified columnar epithelium.

Assuming the student has studied cells properly and developed some confidence in recognizing the shapes of cells and nuclei, this method will inevitably give the correct identification of the section. The student should practice this routine until the order of the procedure becomes automatic.

STUDY OF CONNECTIVE TISSUES

In dealing with the connective tissues we must be cognizant of the elements characteristic of connective tissues: cells, fibers, and matrix. Mesenchyme or developing fibrous connective tissue is characterized by having relatively many cells, few fibers and a fluid matrix. On the other hand, adult fibrous connective tissues have relatively few cells and their identification depends for the most part on their fibers. In cartilage and bone the matrix dominates the picture. The cells are usually well separated and lie in spaces (lacunae) in the matrix.

Only three kinds of fibers are found in connective tissues: collagenous, elastic and reticular.

Collagenous fibers never occur as single fibers except in the embryonic forms of connective tissues where they are just beginning to form, but are always in bundles. The width of the bundles may vary considerably. If a longitudinal section of a collagenous fiber bundle is observed under high power, the student should be able to see delicate, longitudinal striations along the bundle which represent the individual fibers. The cell is closely applied to the outside of the fiber bundle.

Elastic fibers occur as separate fibers. They are finer than the bundles of collagenous fibers and the nuclei of the cells, therefore, appear closer together and they are more plump than the cells of collagenous tissue.

Reticular fibers are very fine, threadlike strands. In combination with collagenous and elastic fibers, they require selective stain for identification. Their presence in glands, tunica propria and in other locations should be observed in specially stained sections.

The appearance of the matrix varies according to its density. In the fibrous connective tissue, where it was fluid, it appears in sections as white spaces among the cells and fibers. In cartilage and bone, the matrix dominates the picture and its density may be so great as to hide the presence of the fibers embedded in it (hyaline cartilage and bone) or at least partially mask them (elastic cartilage).

Fibrous Connective Tissues

MESENCHYME. Examine, with low power, a section through the head of an early chick or pig embryo and locate the cells which lie between the external layer of epithelium and the thick-walled neural tube. Change to high power and observe the structural details of these cells. Search the area until you find a stellate-shaped cell which is typical of these cells of the primitive mesenchyme. Note: the shape of the cells; the shape and relative size of the nuclei. Is the chromatin material of the nucleus dense, vesicular, or granular in appearance? Is the cytoplasm granular? Observe the delicate, branched processes of the cells which are not only in contact with one another, but appear to anastomose and form a continuous protoplasmic structure (syncytium) throughout the tissue. Note the clear, intercellular spaces which, in the living condition are occupied by fluid which forms the ground substance or matrix of the tissue.

Examine a section of the head of an advanced embryo of a pig with the low power. Find an area in which mesenchyme is being transformed into a definite connective tissue. Such an area can usually be found in the region about the developing tooth. Study the tissue with high power. Note: the connective tissue cells, observing that they closely resemble the cells of mesenchyme; in what ways do these cells differ from mesenchymal cells? Compare with the previous slide. Is there more or less intercellular space in this older tissue than in mesenchyme? Observe the presence of delicate fibers in these intercellular spaces. Do these fibers appear to have any special arrangement? Are the fibers single or can you find some which have united to form fiber bundles? What does the presence of fiber bundles indicate?

EMBRYONAL CONNECTIVE TISSUE. Examine a section through the umbilical cord with the high power. Observe the details of the cells and compare them with the cells of the embryonic forms of connective tissue. In the living condition, the intercellular spaces contain a mucoid substance (Wharton's jelly). Note the bundles of delicate fibers, observing the wavy arrangement of the fibers in the bundles. Notice that the intercellular spaces are almost completely filled with these bundles, an arrangement which adds greatly to the strength of the tissue.

In suitably prepared sections, fine, stiff fibers (fibroglia or border fibrils) may be seen passing through the borders of the cells and extending into their processes. Examine a section which has been prepared for demonstrating fibroglia and draw these fibers showing their relation to the cells.

RETICULAR CONNECTIVE TISSUE. With the high power, examine a section of a lymph gland from which the lymphocytes have been removed, thereby revealing the tissues which form the framework of the gland.

Note the connective tissue capsule and the trabeculae which extend from the capsule into the gland. What kind of connective tissue fibers predominate in these structures? Observe the numerous, rodlike nuclei of the connective tissue cells between the fiber bundles in the trabeculae. After locating an area from which the lymphocytes have been removed, shift to high power and examine. Observe the delicate fibers which form a network (reticulum) that fills the spaces between the trabeculae. Note that this network is formed by the reticular cells and their delicate, anastomosing processes. The reticular fibers can be observed most easily in tissues which have been treated with a silver stain (Bielschowsky's technique). In these preparations, the delicate, black stained reticular fibers are seen to lie in close relation to the cells and their processes, and form the true reticulum. These fibers can be traced into the trabeculae where they are seen to be continuous with the collagenous fibers.

Note carefully the structure of the reticular cells. Observe the numerous small cells (lymphocytes) enclosed in the meshes of the reticulum. Only the deeply stained nuclei of these cells are seen. Why?

Make a drawing of a few of the reticular cells as they appear when seen with high power.

FIBRILLAR CONNECTIVE TISSUE. In fibrillar connective tissue the fine white or collagenous fibers (fibrillae) are bound together by a cement substance into bundles (fiber bundles). The most important forms of fibrillar tissue are areolar connective tissue; adipose tissue; dense fibrous tissue; dense elastic tissue.

AREOLAR CONNECTIVE TISSUE. In areolar connective tissue the fiber bundles are interwoven in all directions. Two forms are recognized: dense areolar tissue and loose areolar tissue.

DENSE AREOLAR. With low power examine a section of skin. Locate the tissue (dense areolar tissue) which lies immediately beneath the epidermis. Note the fiber bundles, observing that they are cut longitudinally, obliquely, and transversely. What conclusion, in respect to the direction of the fiber bundles in dense areolar tissue, is to be drawn from the different ways in which they are cut in the section? Change to high power and note the wavy lines which run lengthwise of the fiber bundles. What do they indicate? Note the narrow spaces between the fiber bundles; the rodlike nuclei of the connective tissue cells. What is the relation of the fibroblasts to the fiber bundles? Explain why, for the most part, the cytoplasm of these cells is invisible.

Draw: showing the appearance of dense areolar tissue as seen in the section.

Loose Areolar Tissue. With the low power, examine the part of the section which lies deep to the dense tissue just examined. Note that the bundles of collagenous fibers are gathered into trabeculae, between which are wide interspaces. Note that the trabeculae branch, the branches uniting and forming a loosely arranged network. Why is this tissue called loose areolar tissue? Observe the aggregations of fat cells (adipose tissue) which fill the interspaces between the trabeculae.

Draw showing the characteristic appearance of the tissue as seen in the section.

Examine, with the low power, a section of skin from the palm of the hand which has been stained with an elastic tissue stain (Verhoeff's stain). The collagenous fiber bundles stain pink, while the elastic fibers are a dense blue or black.

Note the arrangement of the elastic fibers among the bundles of collagenous fibers: the branching of the elastic fibers; the anastomosing of branches and fibers to form a network in the meshes of which the collagenous fiber bundles are located. In what parts of the tissue are the elastic fibers the least abundant? In what parts of the tissue are they the more delicate? In what parts of the tissue are they coarser and most abundant? Do any of the elastic fibers extend among the fat cells?

Draw a portion of the section showing the distribution of elastic fibers as they appear when stained with an elastic tissue stain.

ADIPOSE TISSUE. The relation of adipose tissue to loose areolar tissue has already been observed.

With the low power, examine a piece of omentum treated with osmic acid. Note the globular fat cells which have been blackened with osmic acid. Are these cells all the same size? What is the reaction of fats to osmic acid? Observe that these cells are grouped about a blood vessel and its tributaries.

With the high power, examine groups of fat cells in a section stained with hematoxylin and eosin, which contains a considerable amount of loose areolar tissue. Note the manner in which the shape of the cells has been altered by mutual pressure. In most preparations the outlines of the fat cells are modified by the shrinkage resulting from the action of the reagents employed in fixing and hardening the tissue. Observe that the fat which filled the bodies of these cells has been dissolved, leaving a clear space surrounded by a thin protoplasmic membrane which outlines the cells. Observe the nuclei of the fat cells, noting their position at one side of the cell when present in the section. Why are nuclei not observed in connection with all of the cells in the tissue? Nuclei which can be seen in surface view are more or less oval in outline; those which are seen in side view appear flattened and rodlike. Note the small amount of granular cytoplasm which surrounds each nucleus. What gives these cells a "signet-ring" appearance? Observe the trabeculae of fibrous tissue by which the fat cells are supported; also the delicate connective tissue fibers which extend from the trabeculae between the cells. Considerable difficulty may be experienced in distinguishing between the nuclei of the fat cells and those of the cells in the connective tissue.

Draw: showing the appearance and arrangement of the cells in adipose tissue.

With the low power, examine a section of adipose tissue in which the blood vessels have been injected. Observe the location of the principal arteries in the larger septa, their branches following through the smaller septa to break up into capillaries which lie in close relation to the fat cells.

DENSE FIBROUS TISSUE. Dense fibrous tissue differs from dense areolar tissue mainly in the arrangement of the fiber bundles. In all forms of areolar tissue the bundles are interwoven in all directions, while in dense fibrous tissue the bundles lie parallel to one another. In certain forms of dense fibrous tissue (aponeuroses), the parallel bundles in one plane lie at right angles to the parallel bundles in adjacent planes. In tendon all of the fiber bundles are parallel.

Examine a cross section of a tendon with the low power. Note: the layer of connective tissue by which the tendon is enclosed, the tendon sheath (external peritendineum); the connective tissue septa which extend into the tendon from the sheath (internal peritendineum), and which surround the secondary bundles or tendon fasciculi.

The primary bundles (fiber bundles) are outlined by the "winged" tendon cells. A number of primary bundles, surrounded by the delicate septa of the internal peritendineum (the fascicular sheath) is known as a secondary bundle. Secondary bundles may be enclosed by still broader septa, forming a third group, the tertiary bundles.

Note that the connective tissue of the internal peritendineum provides the pathway by which the blood vessels and nerves pass to the different parts of the tendon.

Draw a portion of the section as observed. Show the manner in which the primary bundles are grouped to form secondary bundles, and the relation of the connective tissue septa to the general structure of the tendon.

With the high power, examine a portion of a tendon which has been first macerated, then teased and stained. Note the separation of the fiber bundles; also the separation of the fibers of which the bundles are composed; the position of the tendon cells between the bundles. What is the shape of the nuclei of the tendon cells? How are they arranged? In places where the fiber bundles are well separated, some of the tendon cells may be seen in surface view. Note their irregular outline and large, oval nuclei.

Draw: showing the relation of the fibers to the fiber bundles; the relation of the fiber bundles to the tendon; the form and position of the nuclei.

Examine the longitudinal section of a tendon with the low power. Note: the parallel arrangement of the fiber bundles, and the shape and arrangement of the nuclei. Shift to high power. Observe the longitudinally striated appearance of the fiber bundles. What causes this striated appearance? Note: the septa of delicate collagenous fibers between groups of primary bundles, forming secondary bundles. Are there any blood vessels in these septa? Can nerve fibers be identified in the septa? Note the difference in the form of the nuclei of the connective tissue cells of the septa and those of the tendon cells.

Draw. showing the appearance and structure of a tendon as seen in longitudinal section.

First with low power and then with high power, examine a cross section of tendon. Note: the position of the tendon cells between the primary bundles (fiber bundles), observing their "winged" appearance; the portion of the internal peritendineum which forms the fascicular sheath; the presence of blood vessels and nerves in the fascicular sheath.

Draw a secondary bundle showing the above named parts of the structure.

DENSE ELASTIC TISSUE. The best method of studying dense elastic tissue is to compare preparations of the ligamentum nuchae of an ox, step by step, with similar preparations of tendon.

Examine the teased, unstained fibers of the ligamentum nuchae with high power. Note the size of the elastic fibers, which are not to be compared with the fiber bundles (frequently regarded as fibers) in the tendon, but with the fibers of which the bundles are composed.

Observe the bright, highly illuminated appearance of the elastic fibers. This is due to their high refractive quality, a quality which collagenous fibers do not possess. Do these fibers branch? Note the tendency of the fibers to bend or curl at the points where they are cut or broken. Why do they do this?

Draw a portion of the preparations, showing the characteristics of elastic fibers.

Examine a longitudinal section of ligamentum nuchae with the low power. Note that each fiber is smaller than the fiber bundles in the longitudinal section of a tendon. Each fiber is surrounded by a network of delicate collagenous fibers by which the elastic fibers are bound together. Note that here and there in the section, somewhat larger accumulations of collagenous tissue may be seen. These are extensions of connective tissue from the sheath by which the structure is enclosed. What is the purpose of this connective tissue? How may this be determined by observation? Why does the dense elastic tissue have a more richly nucleated appearance than the dense collagenous tissue? Compare the shape of the nuclei of the elastic tissue with those of tendon.

Draw: showing the appearance of the section as observed.

Examine a cross section of the ligamentum nuchae first with low power and then with high power. In this section the ends of individual fibers, not of fiber bundles (as in the cross section of a tendon), are being observed. Note the varying sizes of the fibers, the smaller fibers being round or oval, while the larger fibers appear more or less triangular in outline. Identify the sheaths of delicate collagenous fibers by which the elastic fibers are surrounded. Observe the nuclei of the tissue cells between the fibers. How do the cells of elastic tissue differ from those observed in the cross section of a tendon?

Draw: showing the appearance and structure of the section as observed.

STUDY OF CARTILAGE

HYALINE CARTILAGE. Examine fresh pieces of articular cartilage, costal cartilage and tracheal cartilage. Note that they resemble each other in being firm and resilient; that they are bluish white in color; and that they have a pearly luster. Cut a thin slice of cartilage and place the slice over the letters on a printed page. Can the letters be seen through the cartilage? Hold the slice to light and observe its capacity to transmit light. What term should be applied to cartilage in view of these observations? Treat the cartilage with a dilute solution of sodium hydroxide. Examine the cartilage after the solution has acted upon it for a short period. Are fibers apparent in the matrix? If so, what is their arrangement?

Three types of hyaline cartilage are recognized: *embryonic*, *adult*, and *old*. The student must realize that these types are not specific or static, but represent stages in a series of progressive changes which take place with the growth of the tissue and as age advances.

EMBRYONIC HYALINE CARTILAGE. Using the low power, examine the head *(epiphysis)* of one of the long bones of a fetal animal. Note the hyaline cartilage which forms the epiphysis. Observe its homogeneous character. In this stage the matrix is more of the precartilage type, hence it is softer and less modified in its different parts. Observe the number, shape and arrangement of the cells. Compare this section with a section of adult cartilage. How does the number of cells present in a given area of embryonic cartilage compare with the number present in a similar area of adult cartilage? In the embryonic cartilage note that the long axes of the cells at the periphery of the cartilage are parallel with the surface; the long axes of the cells in the deeper portions of the matrix are more or less radial in direction. Note that the cells in the deeper portions of the matrix are more widely separated than those nearer the periphery. This is due to interstitial growth—the formation of matrix between the cells. Are any of the cells in groups? If so, in what part of the matrix? Can cartilage capsules be seen surrounding the lacunae? Observe the perichondrium. What is the staining reaction of its fiber bundles? Does the perichondrium completely surround the cartilage? If not, to what part of the cartilage is it limited? Explain the condition observed. Trace the fibers of the perichondrium into the cartilage. What changes are to be observed as the fibers extend more deeply into the matrix? Explain the inclusion of these fibers in the matrix. What observable facts support this explanation?

ADULT HYALINE CARTILAGE. With the low power examine a section through a costal cartilage of a young adult. Note: the perichondrium, observe the staining reaction of its fiber bundles; the form of the nuclei of its connective tissue cells; the cells in the peripheral layers of cartilage immediately beneath the perichondrium. Trace the transition from the connective tissue cells in the perichondrium to the cartilage cells in the peripheral portions of the sections. How are these cartilage cells to be distinguished from the cells in the perichondrium? Identify a lacunae. Note the increase in size of the lacunae from the periphery to the deeper parts of the matrix. Find two cells which are separated by a thin partition of cartilage; also two similar cells which are separated by a considerably broader partition. Explain. Observe the highly refractive quality of the cartilage immediately surrounding the lacunae *(cartilage capsule; territorial cartilage);* the matrix between the cartilage capsules *(interterritorial cartilage).* What is the difference in the staining reaction of the territorial and interterritorial areas? How can you explain this? In the deep portions of the matrix, note groups of cartilage cells which have not separated after cell division has taken place. How do these cells differ from those in the superficial portions of the cartilage? Observe the deep blue color of the matrix between many of the cell groups. What does this indicate? What may be its possible relation to the conditions observed in the cells?

Study the cells with the high power observing their changes in form and arrangement from the perichondrium to the deep portions of the matrix.

OLD HYALINE CARTILAGE. Using first the low power and then the high power, examine a section from the costal cartilage of an aged subject. Note: the extent to which the perichondrium has diminished in thickness; the lack of newly formed *(embryonic)* cells; the number of cells which show degenerative changes in the cartilage immediately below the perichondrium; the arrangement of these cells in groups; the relatively small number of cell groups and their wide separation throughout the matrix; the absence of clearly defined cartilage capsules. What do these observations indicate concerning the activity of the cartilage cells? What conclusions are to be drawn regarding the processes of growth in old cartilage? What observation leads to the conclusion that calcification is characteristic of cartilage in old age?

Draw: characteristic areas to illustrate the structural differences between embryonic, adult, and old hyaline cartilage.

ELASTIC CARTILAGE. Examine a section through the cartilaginous plate that supports the pinna of the ear, using the low power for a general study of the section and the high power for a more detailed study of the cells and fibers. A section stained with Verhoeff's elastic tissue stain provides the best material for this study.

Note the perichondrium, observing the collagenous fibers which are stained pink, and the elastic fibers which are stained a deep black. Trace the elastic fibers from the perichondrium into the peripheral portions of the cartilage. Do the collagenous fibers also extend into the matrix? Note: the size and shape of the cartilage cells; the shape of the lacunae which they occupy; the highly refractive cartilage capsules which surround the lacunae. Do the cells tend to form groups as in hyaline cartilage? What does this indicate regarding the frequency of cell divisions in elastic cartilage? What does it imply regarding the supply of nutritive elements to these cells; the consistency of the matrix? Observe the number and arrangement of the elastic fibers in the deeper portions of the matrix. Are elastic fibers present in the cartilage capsules? To what conclusion does this point concerning the origin of the elastic fibers? Find areas in the cartilage from which elastic fibers are absent and compare with adult hyaline cartilage. Examine some of the cells in elastic cartilage with the high power. Compare them with the cells observed in the deep portions of the matrix in hyaline cartilage. What differences are to be noted?

Draw: (1) the section as it appears with the low power; (2) a number of the cartilage cells as observed with the high power.

Examine a section of elastic cartilage stained with hematoxylin and eosin with the high power. Identify the elastic fibers in the matrix. By what property of elastic fibers are they to be distinguished?

Draw: showing the characteristic appearance of the section.

FIBROUS CARTILAGE. Examine with the high power a section passing through two adjacent vertebrae from a fetus. Note: the fibrous tissue passing from one vertebral body to the other; the fiber bundles which, passing from this tissue, extend between the vertebrae; the rodlike nuclei of the connective tissue cells between the fiber bundles. Note the change in the character of the nuclei of these cells as the fiber bundles enter the region of the intervertebral disc, observing the round spaces *(lacunae)* which they occupy in this region.

The formation of the matrix in which the fiber bundles and cells are embedded prevents the bundles from pressing on the cells, hence the rounded form, rather than the flat, compressed form characteristic of the nuclei in the fibrous tissue. The matrix is softer, more resilient, and more transparent than in the cartilages previously studied.

Follow the fiber bundles in the fibrous cartilage of the intervertebral disc, noting the manner in which they disappear in the embryonic cartilage of which the vertebral bodies are formed. In the adult condition the fiber bundles are lost in the same way in the articular cartilages with which they are associated.

Draw: showing the relation of the tissue forming the intervertebral discs to the vertebral bodies and the transition in the form of the nuclei from the fibrous connective tissue to the fibrous cartilage.

Examine with the high power a section from the intervertebral disc of an adult. Note: the parallel arrangement of the collagenous bundles; their wavy course in the tissue; the clearness with which they can be seen, giving them a close resemblance to a section of tendon; the large, round lacunae in which the cartilage cells are located; the linear arrangement of the cells, comparing their arrangement in fibrous cartilage with that observed in dense fibrous tissue *(tendon)*. Do the cells of fibrous cartilage tend to form in cell groups?

Draw: showing the characteristic appearance of the tissue.

STUDY OF BONE

GROSS STRUCTURE OF BONE. (1) Examine one of the long bones *(humerus* or *femur)* which has been sectioned longitudinally. Observe the solid *(dense)* appearance of the bone surrounding the marrow cavity in the diaphysis; the spongy bone which more or less completely fills the epiphyses, noting the latticelike arrangement of the trabeculae and spicules of which it is formed; the thin, shell-like layer of dense bone by which the spongy bone is enclosed.

(2) Examine an irregular bone *(metacarpal; metatarsal* or *body of a vertebra)* which has been sectioned. Note that the structure of the entire bone is similar to that of the epiphyses of the long bone; i.e., it consists of a mass of spongy bone with a thin, outer covering of dense bone.

(3) Examine the sectioned surface of a flat (*parietal*) bone. Note the inner and outer plates of dense bone between which a narrow layer of spongy bone *(diploë)* is to be seen.

Draw: showing the architecture of each type of bone examined.

DECALCIFIED BONE. With the low power, examine a cross section of a long bone (preferably of a small animal) which has been decalcified. Identify the thin layers or lamellae of bone which completely encircle the bone at its circumference *(external circumferential lamellae)*; similar lamellae which occupy the portion of the bone surrounding the marrow cavity *(internal circumferential lamellae)*. Are lacunae found in relation to these lamellae? Are Haversian canals found in this area? Identify an Haversian canal; lacunae, the numerous small spaces concentrically arranged about each Haversian canal; concentrically arranged bony lamellae. Each Haversian canal, with its encircling group of lacunae and bony lamellae, constitutes an Haversian system. In the area between the external and internal circumferential lamellae, find lacunae which do not belong to any of the Haversian systems. These lacunae belong to the interstitial lamellae. In some cases the lamellation of the bone is apparent in decalcified material; in other cases, the formation of the lamellae is masked by the character of the matrix.

Identify the periosteum. Of what is it composed? Follow the course of any fibers which can be traced from the periosteum into the substance of the bone. What are these fibers called?

Observe the marrow cavity.

Draw: showing the appearance of the bone as seen in a decalcified section.

DRY SECTION OF DENSE BONE: CROSS SECTION OF DRY BONE. (1) Examine the section with the low power. Observe the Haversian systems, each consisting of a series of concentric lamellae enclosing an Haversian canal; the lacunae or spaces in which the bone cells are located in living bone. Observe that the general arrangement of the lacunae follows that of the concentric lamellae. Observe the canaliculi, seen as fine, dark lines extending from the lacunae through the bony substance of the lamellae. Here and there in the section, canals similar to the Haversian canals may be seen passing from one Haversian canal to another. Observe the arrangement of the Haversian systems in relation to one another, noting the interstitial lamellae between the Haversian systems with their associated lacunae and canaliculi.

Air is imprisoned in the Haversian canals, lacunae, and canaliculi by the medium in which the section is mounted. The difference in the refraction of the light passing through these air-filled spaces and of that which passes through the matrix of the bone causes them to appear as dark areas or lines against a lighter background.

Draw: the section as seen with the low power.

(2) Examine an Haversian system with the high power. Observe the irregular outlines of the elongated lacunae. What is the position of the lacunae in relation to the lamellae? Are all the lacunae in this relation? Observe the delicate lines by which the concentric lamellae are outlined. Note the canaliculi extending from the lacunae; their branching; the anastomosing of their branches. Follow the course of the canaliculi from the lacunae nearest an Haversian canal. Do any canaliculi reach the canal? Observe the interstitial lamellae. Is there any relation between the lacunae in the interstitial lamellae and those in the peripheral portions of the Haversian systems?

Draw: showing the structures and their relations as observed in an Haversian system.

Longitudinal Section of Dry Bone. Study the section with the low power. Identify the Haversian canals; the bony lamellae by which each canal is encircled; the lacunae and canaliculi. To what conclusion as to the length of an Haversian system does the above observation lead? Observe the canals which pass from one Haversian canal to another.

Draw: showing the structure of bone as seen in longitudinal section.

From the foregoing observations, construct a diagram showing the manner in which blood vessels and nerves are distributed to the different parts of the bone.

STUDY OF INTRAMEMBRANOUS BONE FORMATION

The best material for the study of the earliest stages in the development of intramembranous bone is provided by a series of sections through the parietal bones in various stages of development. With the low power magnification locate an area where bone is being formed. Shift to high power and focus on the margin of an area of newly formed bone. Observe the narrow, platelike deposit of preosseous material (ostein; osteoid) which lies between the bony segments and the adjacent connective tissue. Note the hyaline appearance of this ostein. How does it stain? Note the connective tissue fibers which are associated with it and which are apparently lost in its substance. Identify the bone forming cells (osteoblasts). Note the shape and staining reaction of these cells. What is the position of their nuclei? Where are these cells located? What is their relation to the fibroblasts of the adjacent connective tissue? From their location can you tell anything about the direction in which the bone is growing? Explain. Find cells which are partly embedded in the matrix. How do these cells differ in form from the more active osteoblasts? Observe the cells which are wholly embedded in the substance of the bony plates. What is the shape of these cells? What are they called? Find one or two osteoclasts. How do they compare with the osteoblasts in size? In staining reaction? In the number of nuclei they possess? What is the character of the tissue surrounding the bony plate?

Draw: showing the appearance and arrangement of the structures in developing bone.

Examine a section of parietal bone at a more advanced stage in its development. Use the low power for a general study of the section, and the high power for observing details of structure.

Note that the bone on the inner (cerebral) side has assumed the character of dense bone by the development of concentric layers of bony tissue in the spaces between the spicules. Observe the atypical character of these Haversian systems. Note Haversian spaces in which the development of concentric layers has been only partially accomplished. In most sections, at this stage in the development of the bone, the manner in which dense bone is formed can be followed from the Haversian spaces to the systems where the concentric layers surround the blood vessels.

Observe the spicules which are being formed at the outer (cranial) surface of the bone, noting the lighter area of uncalcified material which borders the more deeply colored, ossified portion of the bone. As in the previous study, observe the osteoblasts arranged along the uncalcified borders of the spicules. Note areas on the surface of the bars and spicules where there is no uncalcified border. What is the form of the osteoblasts in these areas? Note the fibers radiating from the spicules into the surrounding tissue; the transformation into osteoblasts of the connective tissue cells associated with these fibers. Find a number of osteoblasts which are becoming osteocytes by having matrix deposited about them. Note where two spicules are pointed toward each other, and the fibers that pass from one spicule to the other; the osteoblasts which are arranged along these fibers. What does this indicate concerning the manner in which Haversian spaces are formed? Find a number of osteoclasts. On what surface of the bone are they located? Explain their presence on this surface. Identify the external periosteum; the internal periosteum. What tissue, previously studied, does the osteogenetic layer of the periosteum resemble?

The cells and fibers of the osteogenic layer of the periosteum form bone in the region of the spicules; when enclosed in the Haversian spaces they become primitive marrow. Tissues which are capable of more than one functional activity are said to be *multipotential.*

STUDY OF ENDOCHONDRAL BONE FORMATION

With a hand magnifier examine a section of a phalanx from the finger of a fetus. Note: the epiphyses, the embryonic cartilage appears yellowish or light blue while the presence of calcified cartilage is indicated by the areas which are stained a deep blue. Identify: the diaphysis or shaft which is located between the epiphyses; the marrow cavity which occupies the mid-portion of the diaphysis. How do the segments of decalcified bone stain?

Using the low power, follow the changes which take place in the cartilage preliminary to its replacement by bone; the formation of the primary marrow spaces. How are the primary marrow spaces to be identified? Note the areas in which bone has been deposited on and within the phalanx.

Observe the embryonic character of the cartilage of which the epiphyses are formed; the layer of connective tissue on the sides of the epiphyses (perichondrium). What is the extent of the perichondrium? What surface does it leave uncovered? Note the evidence of calcification in the cartilage. In what parts of the cartilage does calcification occur? Note in the calcified area, the changes which take place in the cartilage cells: their tendency to form parallel rows. Compare these cells with the cells in the calcified portion of adult cartilage. What possible relation may there be between the calcification of the cartilage and the observed changes in the cartilage cells? Note the enlargement of the lacunae which these cells occupy, also the formation of primary marrow spaces by the resorption of the walls between the lacunae. The calcified cartilage separating the rows of cartilage cells remains in the form of spicules between the primary marrow spaces. Observe the bone which has been deposited on these spicules; the osteoblasts located on the borders of the newly formed bone; spicules which have the appearance of lying freely in the marrow cavity. How is the cartilage which forms the core of the spicules to be distinguished from the bone by which it is surrounded? Note: the layer of subperiosteal bone forming the wall of the diaphysis; the periosteum, identifying its osteogenetic layer. Find points where the osteogenetic tissue, conveying a blood vessel (periosteal bud), has entered or passed through the subperiosteal bone. Note the spaces filled with primitive marrow that are in the subperiosteal bone. What spaces previously observed do they resemble? What do these spaces suggest as to the manner in which subperiosteal bone is formed? Observe the difference between the marrow in the secondary marrow space (marrow cavity) and the osteogenetic tissue (primary marrow) in the primary marrow spaces. In what does this difference principally consist?

Draw the section in outline and fill in the details observed in following the above laboratory procedure.

Examine the section with the high power. Observe the differences between the cells of the embryonic cartilage in the epiphysis and those in the calcified portions of the cartilage. What is the nature of these differences? Observe one of the spicules between the primary marrow spaces, noting the calcified cartilage and the bone by which it is bordered. How does this bone compare with that observed in the early stages of intramembranous bone formation? Observe the osteoblasts arranged along the surface of the newly formed bone. From what tissue are the osteoblasts obviously derived? Examine an area in which the subperiosteal bone is thickest. Is there any evidence of its being deposited in layers (lamellae)? Identify the osteoclasts which may be found in relation to the spicules and also on the inner surface of the subperiosteal bone. Note the difference between the osteogenic tissue in the primary marrow spaces and the tissue which occupies the secondary marrow space or marrow cavity. What appears to be the principal function of the osteogenic tissue? Of the tissue occupying the marrow cavity? Can cells resembling osteoclasts be found in the tissue of the marrow cavity apart from bone? What does this suggest as to the possible origin of osteoclasts? Identify a periosteal bud. Of what does it consist?

Make several drawings to show the structural details indicated in the above outline.

METHOD OF IDENTIFICATION OF CONNECTIVE TISSUES

The identification of connective tissues requires recognition of not only cells, but fibers and matrix as well. Given an unknown slide, the student should first examine the tissue under low power and notice which of these three elements predominate: cells, fibers or matrix.

If there are numerous cells with relatively few fibers, or if the fibers are relatively numerous but not arranged in parallel rows, the tissue is probably mesenchyme or embryonal connective tissue. Next observe the shape of the cells and the number and arrangement of the fibers present. If the cells are closely arranged, stellate in shape *with anastomosing processes and no fibers are apparent in the matrix*, it is undoubtedly very young mesenchyme. If, on the other hand, the cells are farther apart, stellate in shape, the processes less prominent and not anastomosing and there are single fibers apparent in the matrix, the tissue is old mesenchyme (called embryonic connective tissue by some authors). Embryonal connective tissue is characterized by stellate-to oval-shaped cells which are rather widely separated, fibers arranged in bundles, the bundles not being arranged in any regular fashion, and the matrix is scarcely apparent since it is now completely filled by the fiber bundles.

The above characteristics of early connective tissues can be remembered if the student realizes that the characteristics represent logical changes which result from growth and development. At first cells are numerous and their processes anastomose and form a syncytium, and they are bathed in a relatively abundant fluid matrix. With growth of the organism, the cells become more widely separated, their processes no longer anastomose and as a result the cells become more oval in shape. Fibers begin to be found singly at first and later, as they become more numerous, they are arranged in bundles. These fibers are formed in the matrix and as they increase in number, the matrix is no longer apparent. So the presence, number, and arrangement of the fibers is a gauge to the age of the developing connective tissue.

If on first examination the student observes that fibers seem to predominate in the tissue, it is very probable that he has a section of fibrous connective tissue and he must differentiate between areolar, dense fibrous (tendon), or dense elastic (ligamentum nuchae) connective tissue. The areolar connective tissues are characterized by bundles of fibers that are interwoven into a compact feltlike mass. The cells are scattered and are arranged on the edge of the fiber bundles. The terms dense and loose areolar are used to designate the quantity and compactness of the fiber bundle mass. Loose areolar tissue usually consists of strands or trabeculae of areolar tissue and is always associated with quantities of fat (if the fat cells are abundant, it is usually referred to as adipose tissue).

In both dense fibrous and dense elastic connective tissue, the fiber bundles are arranged in parallel. They should offer no particular difficulty to the student if he remembers that collagenous fibers (in tendon) always occur in bundles and that elastic fibers (in ligamentum nuchae) always occur singly. Therefore, in longitudinal sections of tendon the parallel fiber bundles are relatively wide, the cells which are located at the periphery of the bundles are farther apart and will be fewer than in a section of ligamentum nuchae where they are located between the individual fibers. Moreover the appearance of the nuclei of the cells is typical in each tissue. In tendon the nuclei appear as relatively long, narrow, dark staining structures with "squared" ends resembling a series of "dashes." The nuclei in ligamentum nuchae are shorter, more oval and less deeply stained. Some students confuse tendon with striated muscle. This is a careless error since striated muscle presents cross striations, the nuclei are larger and more oval.

Identification of cross sections of tendon and ligamentum nuchae can be made without too much difficulty. Again in tendon the nuclei are farther apart, the fiber bundles appear rather distinctly, and the cells have a characteristic "wing-shape." The connective tissue septa dividing the tendon into primary and secondary tendon bundles are very distinct. In ligamentum nuchae the cross section appears to have a more homogeneous appearance. The nuclei of the cells are closer together and oval in shape. The connective tissue septa are fewer and less distinct.

Reticular connective tissue should not be hard to identify if the student remembers that reticular tissue always forms the stroma of lymphoid organs. This tissue when stained with hematoxylin and eosin appears as a delicate reticulum of faintly staining stellate shaped cells with anastomosing processes and fine reticular fibers. If the tissue has been stained with silver the delicate reticular fibers will stain black. There will almost always (even in washed tissue) be many lymphocytes caught and stained in the reticular fiber meshwork and this will aid the student in his identification.

Adipose tissue always occurs in connection with loose areolar tissue which forms the supporting framework for the fat cells. The fat cells are large cells in which, in most instances, only the cell membrane is apparent. In ordinary sections the fat has been dissolved out during the preparation of the tissue, thus leaving large empty spaces. Some of the cells will be cut so that their nuclei and a small amount of cytoplasm surrounding the nuclei will show. The cytoplasm and nuclei will have the characteristic compressed, new-moon shape which has given the cells their so-called signet-ring appearance.

If the matrix is the dominant element, it is likely the tissue is cartilage or bone. To make certain one looks for the presence of lacunae. If they are present, it is one of these two tissues. In order to differentiate between cartilage and bone, look for the presence of Haversian systems which are characteristic and diagnostic of bone. If no Haversian systems are present, it is cartilage and the student must differentiate between hyaline, fibrous and elastic. Eliminate the easiest one first, this is fibrous cartilage. In adult fibrous cartilage the fibers are arranged in wavy, parallel bundles. The cartilage cells lie in lacunae between the fiber bundles and therefore have a definite linear arrangement.

If, on the other hand, the matrix has a relatively homogeneous appearance (when stained with hematoxylin and eosin) it is either hyaline or elastic cartilage. Next observe the shape and arrangement of the cartilage cells. If the cells and lacunae are quite oval, occur for the most part singly, and are uniformly scattered through the matrix, it is elastic cartilage. Sometimes with hematoxylin and eosin stained tissue it is possible to observe the elastic fibers as a final identifying characteristic. If the section is stained by one of the elastic tissue stains, the elastic fibers stand out sharply as fine black fibers interwoven throughout the matrix.

Hyaline cartilage cells are flattened to round oval and occur singly and in groups. The younger, more flattened cells usually occur singly. In older hyaline cartilage several cells may occur within the same lacunae, being separated by thin strips of cartilage. Other distinguishing characteristics of hyaline cartilage to be observed are the territorial and interterritorial areas and the capsules. The presence of these features should be checked before final identification of hyaline cartilage is made.

STUDY OF BONE MARROW

Material for the study of bone marrow may be provided either by sections or smears. Sections give the best picture of the arrangement of the myeloid elements, but for the identification of the different cell types a smear preparation, stained with either Wright's or Giemsa's blood stain, is best.

Examine a section of the epiphysis of a long bone of a rabbit with the high power (after the first examination with the high power has been made the oil-immersion objective should be used). Observe the distribution of the cells of the red marrow between the spicules of bone. With some exceptions the identification of the cell types is difficult, owing to the manner in which their staining properties have been modified by the decalcifying fluids and other reagents employed in making the section. Following the foregoing description, identify as many of the cell types as possible. Note the large, circular spaces (fat cells) which appear here and there in the tissue.

Examine a smear preparation of bone marrow, using the oil-immersion objective. Owing to the difficulty of obtaining human material, marrow from the epiphyses of the long bones of a monkey (if possible), or a dog, may be used.

It should be borne in mind that preparations of marrow from one of the lower animals give only an approximate picture of the condition obtaining in human marrow.

Observe the different types of cells to be found in bone marrow, as follows:

MYELOCYTES. These are the most numerous cells of the marrow. They are to be recognized as neutrophilic, eosinophilic, and basophilic myelocytes by the presence of the granules which are characteristic of these cell types. Note the large, slightly indented nucleus. Forms in which the cytoplasm is decidedly basophilic and in which only a few granules appear, are to be regarded as promyelocytes. As a rule, only a few promyelocytes are to be found in these preparations. Observe cells which are somewhat smaller than the myelocytes, and in which the nucleus is deeply indented or crescentic; having, also, a cytoplasm which is filled with granules—metamyelocytes. The metamyelocytes do not divide but are transformed directly into mature leucocytes.

MATURE GRANULOCYTES. These cells are similar to those which have already been observed in the blood. They are to be recognized by the staining properties of their granules as neutrophils, eosinophils and basophils. Note the characteristic lobulation of their nuclei. Which type is most numerous? Which type is least numerous? Does the same observation apply to the myelocytes?

HEMOCYTOBLASTS (MYELOBLASTS). Only a few of these cells occur in preparations of normal bone marrow. When present they are to be recognized by their large size, their basophilic, nongranular cytoplasm, and large round or oval nuclei which may contain two or more nucleoli. These cells closely resemble large lymphocytes with which they are regarded by many as being identical. They often occur in small groups of three or four cells.

LYMPHOCYTES. A small number of lymphocytes may be observed. Those which occur in the bone marrow are identical with the lymphocytes found in the blood stream. They are to be recognized by their relatively large, deeply staining nuclei about which is a very thin film of cytoplasm.

ERYTHROCYTES. Observe the large number of erythrocytes which are similar to those seen in the study of the blood. Other cells belonging to the erythrocyte series may be observed as follows:

NORMOBLASTS. Cells resembling the erythrocytes, but in which a round or slightly shrunken nucleus may be seen. Note the intensely acidophilic reaction of these cells which is due to the almost negligible amount of hemoglobin present in their stroma. Extruded nuclei may sometimes be observed among the erythrocytes.

ERYTHROBLASTS. These cells are somewhat larger than the normoblasts. They may be recognized by their basophilic cytoplasm which has a slightly reddish tinge due to the increasing amount of hemoglobin present. The chromatin in their large, round or oval nuclei consists of coarse masses arranged in the so-called "checkerboard" fashion. A few procrythroblasts (megaloblasts) may be present. They are slightly larger than the erythroblasts, their cytoplasm being strongly basophilic with an almost imperceptible reddish tinge. The nucleus is large, round and contains two or more nucleoli.

MEGAKARYOCYTES. These cells are conspicuous because of their size, their irregular outline, a clear, nongranular cytoplasm and their large horseshoe-shaped, or ring-shaped, nuclei which are divided by constrictions into numerous irregular lobes.

Draw examples of each of the types of cells observed; grouping the cells so as to show, as nearly as possible, their arrangement in the preparation.

IDENTIFICATION OF UNKNOWN

Identification of blood smears and bone marrow should present no difficulty to the student.

STUDY OF BLOOD

Place a drop of *warm* normal salt, or Ringer's, solution on a clean slide. Wipe the tip of a finger with a piece of absorbent cotton moistened with 80 per cent alcohol. Prick the finger with a sterilized needle and squeeze from it a drop of blood. Add the drop of blood to the solution on the slide. (Wipe the finger again, very carefully and thoroughly with alcohol.) Place a cover slip on the preparation and examine with the high power.

Observe the red corpuscles (erythrocytes) noting that they appear as flattened, straw-colored discs with dark borders surrounding lighter central areas. Find rows of corpuscles which are adhering by their flat surfaces, noting their resemblance to stacks of coin (rouleaux formation). Observe that as the medium in which the corpuscles have been placed becomes dense by evaporation at the edges of the cover glass, the osmotic tension is changed from an isotonic to a hypertonic solution. Note how the corpuscles begin to alter their shape, becoming shrunken spheres, their surfaces being studded with small, knoblike processes (crenated corpuscles). Colorless bodies are to be seen here and there among the red corpuscles. The larger of these present a somewhat irregular outline (leucocytes: white blood cells). The smaller of these colorless bodies are about half the size of a corpuscle and tend to be collected in groups (thrombocytes: blood platelets).

Draw: showing the different forms and arrangements of the red corpuscles as seen in the preparation.

LEUCOCYTES. Blood smears stained with Wright's or Giemsa's blood stains may be used for this study. The staining method suggested here is Wright's.

It is good practice for the student to prepare a blood smear and stain it as part of the laboratory assignment for work on the blood. The procedure is relatively simple and is as follows:

With a piece of cotton wet with alcohol, first clean the tip of the finger. Let the alcohol evaporate completely. Two clean slides should be laid out and ready. With a sterile lancet or needle, prick the finger tip so that it bleeds freely. Place a small drop of blood on one end of one of the slides. This slide should now be picked up and held in the left hand, with the end containing the drop of blood being held firmly between the thumb and ring finger. The other end of the slide should be supported from below by the index and middle fingers. With the right hand grasp the second clean slide. Resting it near the center of the first slide at an acute angle pull it into the drop of blood. The blood should spread along the entire edge of the second slide and the student should then push the second slide quickly along the entire extent of the first slide, thus dragging the blood along in a thin film. DO NOT *PUSH* THE DROP OF BLOOD ALONG WITH THE SECOND SLIDE. Why? If this entire procedure is done quickly and the slides are perfectly clean, a thin blood smear will be evenly distributed *on the first slide. Allow the smear to dry. Stain with Wright's* stain.

Method:

Place the slide flat on a staining rack and flood the smear with 12–18 drops of Wright's stain.

Allow stain to remain one minute.

With a dropper add an equal quantity (12–18 drops) of distilled water to the stain on the slide. A metallic scum should form. Allow the diluted stain to remain on the smear five minutes.

Flood the stain off with water. Do not tip the slide to drain the stain off or the metallic scum will adhere to the smear and ruin it.

Allow the stained slide to dry completely without touching the portion containing the smear. If properly done the stained portion should have a reddish-straw color. When the slide is thoroughly dry, place a drop of cedar oil on the smear and examine it, using the oil-immersion objective.

Identify the following:

ERYTHROCYTES. The most numerous of the structures appearing on the slide. They are to be recognized by their having dark borders surrounding lighter central areas and by their color which varies from a straw color to a brick red. In normal blood the proportion of erythrocytes to leucocytes is about 500 to 1.

LYMPHOCYTES. Lymphocytes can be identified by their relatively large nuclei, filled with coarsely granular chromatin. The nuclei stain a deep blue (almost black) color. The small amount of clear cytoplasm is seen to be more abundant on one side of the nucleus; the remainder of the cytoplasm is in the form of a thin, protoplasmic film by which the nucleus is surrounded.

Large lymphocytes are regarded, clinically, as being absent from the blood stream; when present they are large cells with oval, slightly indented, deeply staining nuclei. The large cells, resembling lymphocytes, which appear in the blood under certain pathological conditions (myelogenous leukemia) are hemocytoblasts (myeloblasts of the clinicians), or the stem cells from which the other elements of the blood are derived.

MONONUCLEAR LEUCOCYTES. These cells may be distinguished from lymphocytes by their greater size, due to their more abundant cytoplasm and by their large, crescentric nuclei. Compare these cells for size and for the intensity of the nuclear stain, with those which have oval, indented nuclei. Which are the larger? In which cells do the nuclei stain more intensely?

GRANULAR (POLYMORPHONUCLEAR) LEUCOCYTES. These are large cells, which are to be recognized by the granules present in the cytoplasm and by their lobated nuclei.

Neutrophilic Leucocytes. These cells are about a third larger than the erythrocytes. They are to be identified by lobulated nuclei—three lobes can usually be observed—and the fine, purple or lilac colored granules with which the cytoplasm is filled. Note the strands of nuclear material by which the lobes of the nuclei are joined together.

Eosinophilic Leucocytes. These cells are somewhat larger than the erythrocytes. Note that their nuclei usually consist of two lobes joined together by a band of nuclear material. Note, also, that the cytoplasm is filled with coarse granules which stain a deep red color.

Basophilic Leucocytes. These cells are only slightly larger than the erythrocytes. Note the coarse, irregularly shaped granules of variable sizes stained a deep blue (almost black) with which the cytoplasm is filled. The nuclei consist of three or more lobes. How do these nuclei stain as compared with the nuclei of other granulocytes? In most basophils the nuclei are almost, if not quite, obscured by the granules.

THROMBOCYTES (BLOOD PLATELETS). Small, non-nucleated, colorless bodies, irregular in outline and about half the size, or less, of an erythrocyte. Note the outer clear zone and the inner core of granular protoplasm, also the manner in which the platelets are clustered in groups.

Draw examples of each type of cell observed in the foregoing study.

Type of Cell	*Diameter in Microns*	*Number per Cubic Millimeter*
Erythrocytes	7-8	5,000,000 male 4,500,000 female
Leucocytes	.....	7,000-10,000
Nongranular leucocytes		
Lymphocytes	7-10	20%
Monocytes	11-20	6-10%
Granulocytes		
Neutrophils	9-12	60-70%
Eosinophils	12-14	2-4 %
Basophils	8-10	0.5-1 %

STUDY OF MUSCLE TISSUES

SMOOTH MUSCLE. First with low and then with high power, examine a preparation of smooth muscle in which the fibers have been separated by teasing. Locate a single fiber that lies apart from the main bit of muscle tissue. What is the shape of the fiber? Note the large, oval nucleus. Where is it located in relation to the fiber? The ends of the nuclei are rounded, but the granular cytoplasm in which they are located, extends beyond the ends of the nuclei and gives them a pointed appearance with ordinary magnifications. Are you able to observe the longitudinal striations in the fiber? What causes this appearance of the fiber? Look for a *fiber which has been broken in the process of teasing* and see if you can identify the myofibrillae extending beyond the body of the fiber. These myofibrillae are enveloped by a fluidlike protoplasmic substance (sarcoplasm) which constitutes the remaining substance of the fiber. Are you able to distinguish a definite membrane enclosing the fiber?

Draw several smooth muscle fibers, showing their form and general appearance.

Examine a section of the muscular portion of the wall of the alimentary canal with the low power.

In the portion of the section in which the smooth muscle fibers are cut longitudinally, note the difficulty in following the outlines of the fibers owing to the manner in which they overlap. In places where the fibers are separated, observe the network of delicate connective tissue fibers between the muscle fibers. Note the deeply stained band, due to *postmortem contraction, which may be seen crossing the smooth muscle* fibers.

In a portion of the section where the muscle has been cut transversely, observe: the arrangement of the fibers in groups or bundles, imperfectly outlined by connective tissue septa; the delicate connective tissue fibers which extend into the bundles from the septa and surround the muscle fibers; the difference in the size and outline of the fibers due to their fusiform shape and being cut at different levels. Those which are cut nearer the ends are smaller and more angular than those which are cut through the level of the nucleus. Note the position of the nucleus in the central portion of the fiber. Does every fiber show a nucleus? Explain. Look for blood vessels and nerves in the septa which provide the pathways by which these structures reach the different parts of the tissue.

Draw: showing the appearance of smooth muscle (1) in longitudinal section; (2) in cross section.

STRIATED MUSCLE. With the high power examine a preparation of striated muscle in which the fibers have been separated by teasing. Note: the shape and size of the fibers; the faintly marked longitudinal striations due to the presence of bundles of delicate myofibrillae (sarcostyles: muscle columns of Kölliker) which extend through the length of the fiber. The sarcostyles may be seen extending beyond the broken ends of some of the fibers. Can the extremely delicate myofibrillae be seen extending beyond the ends of the sarcostyles? Observe the alternating light and dark transverse bands, or cross striations, from which this type of muscle derives its name; the thin, transparent membrane by which the fiber is enclosed (sarcolemma). The sarcolemma can be seen best at points where the fibers have been broken and slightly *twisted. Note the large, oval nuclei which are located at the periphery* of the fiber, and which can be observed to lie immediately beneath the sarcolemma. Note the small masses of granular protoplasm in which the nuclei are embedded.

With the high power examine a longitudinal section of striated muscle stained with Heidenhain's iron-hematoxylin to bring out the cross striations. Note: the alternating light (isotropic) and dark (anisotropic) bands; the dark line which passes through the middle of the light band (Krause's membrane).

For a complete picture of the lines by which the fibers of striated muscle are crossed, preparations of the wing muscles of insects should be examined. In these Hensen's disc (H) and Hensen's line (M) can also be observed.

Draw: showing the appearance of striated muscle in longitudinal section.

With the high power examine a cross section of striated muscle. Note: the connective tissue septa (perimysium) by which the fiber bundles are surrounded; the connective tissue fibers which extend from the perimysium between the fibers in the bundles (endomysium); the individual fibers, each of which is surrounded by a delicate membrane (showing as a dark line) the sarcolemma; the cut ends of the sarcostyles, each of which represents an area of Cohnheim; the narrow, light spaces between the Cohnheim's areas which indicate the distribution of the sarcoplasm in the fiber. Observe the position of the nuclei, which lie directly beneath the sarcolemma. Note if any of the nuclei lie more deeply in the substance of the fiber. What type of fiber does this indicate?

Draw several of the fibers, observing their arrangement, as well as the arrangement of the component parts of the fiber, as seen in the section.

With a low power examine a section of injected striated muscle. Note: the larger vessels which lie in the septa between the muscle bundles; the smaller vessels which end in capillaries; observe the manner in which the capillaries extend lengthwise along the muscle fibers; the shorter capillary branches which pass around the fibers from one of the longer capillaries to another.

CARDIAC MUSCLE. Examine a section of cardiac muscle stained with Heidenhain's hematoxylin. Using the high power observe a portion of the section in which the fibers are cut longitudinally. Note: the form and arrangement of the fibers; their manner of branching, following the branches to their union (anastomoses) with other branches, or with other fibers. This indicates the syncytial character of cardiac muscle. Note the faintly marked longitudinal striations, due to the presence of myofibrillae; the cross striations similar to those observed in striated muscle. Note the difference in the distinctness with which the cross striations appear in the two types of muscle. Observe the sharply defined, dark bands which cross the fibers at irregular intervals (intercalated discs). Observe discs which extend partly, and others which extend entirely, across the fiber; also discs which form a series of steps as they cross the fiber.

Draw showing the characteristics of cardiac muscle as observed.

With the high power examine a few fibers of cardiac muscle which have been cut transversely. Note: the arrangement of the fibers in incomplete bundles; the septa of connective tissue between the bundles (interstitial connective tissue); the position of the nucleus in the central portion of the fiber, observing the granular protoplasm by which it is surrounded; the arrangement of the sarcostyles in rows, which extend from the periphery toward the center of the fiber, noting their arrangement, which resembles the spokes of a wheel. The spaces between the rows of sarcostyles, between the ends of the sarcostyles and the area surrounding the nucleus, are occupied by sarcoplasm. Note the extremely delicate sheath with which the fibers are enveloped.

Draw several of the fibers, showing their structure as observed in cross section.

Compare the section studied with one stained with hematoxylin and eosin. What aspects of the tissue appear the same in both sections? What structures appear in one section which are not clearly visible in the other?

METHOD OF IDENTIFICATION OF MUSCLE TISSUES

The identification of muscle should offer no particular difficulty. Given an unknown slide which consists of a definite arrangement of parallel fibers, a number of nuclei scattered throughout the tissue and practically no matrix. Using the low power first note the shape of the fibers. If they tend to be cylindrical in shape (longitudinal section) it may be striated or cardiac muscle. Shift to high power and observe the fibers for cross striations. If they are present it must be striated or cardiac muscle. Next observe the location of the nuclei. If they are located for the most part at the periphery of the fiber, it is striated muscle. If, on the other hand, the nuclei are centrally located in the fiber, it is probably cardiac muscle. Before final diagnosis, however, the student should check to see if the fibers branch and if intercalated discs are present. Both are diagnostic of cardiac muscle.

Cross sections of these two types of muscle are easily identified. When sectioned transversely, striated muscle fibers appear as distinct fibers of fairly uniform size. The nuclei are located peripherally with few exceptions. In some fibers, areas of Cohnheim can be identified as well as the cut ends of the myofibrillae. When cut transversely, cardiac muscle fibers are about the size and shape of striated muscle fibers. They differ in having centrally located nuclei and in the arrangement of the myofibrillae which are not uniformly distributed throughout the sarcoplasm but are arranged in a linear fashion from the center of the fiber toward the periphery, resembling the spokes of a wheel.

Identification of smooth muscle in longitudinal section presents some difficulty. The individual fibers are spindle-shaped and arranged so closely together that it is difficult to make out either the separate fibers or their shape. The fibers are also narrow with centrally located nuclei so that the tissue has many small, faintly staining, oval nuclei in each section. Under high power, however, the fibers should show longitudinal striations which are due to the longitudinally directed myofibrillae.

Cross section of smooth muscle is easily identified. When cross sectioned, the diameter of the spindle-shaped fibers appears to vary in size since some may be cut through the thick portion, while others are cut toward their tapering ends. Only the fibers of largest diameter show nuclei and they are located in the center of the fiber.

STUDY OF NERVOUS TISSUE

NERVE CELLS. With the low power examine a section of a spinal ganglion. Observe the groups of round or oval cells which occupy the enlarged or ganglionic portion of the section; the nerve fibers passing through the ganglion; a similar group of fibers, which are separate from the ganglionic part, but which are joined to the portion of the nerve trunk in which the other fibers are located. Are any nerve cells associated with this group of fibers?

The ganglion is a part of the dorsal root of the spinal nerve, its cells and fibers being concerned with the transmission of sensory impulses. The bundle of nerve fibers which are separate from the ganglionic portion of the section belong to the ventral root, the fibers of which transmit motor impulses.

Examine the section with the high power. Observe the form and size of different nerve cells in the ganglion; the finely granular character of their cytoplasm; their large, vesicular nuclei, each containing a fine network of chromatin and a deeply stained nucleolus; the flattened cells with prominent nuclei (mantle cells) which form a sort of capsule investing the ganglion cells. A single process may occasionally be found extending from one of the cells. This process can rarely be followed, in sections, beyond the mantle cells. To what class do these cells belong?

Draw: (a) the section as seen with the low power; (b) a number of the ganglion cells, showing their appearance and structure.

Examine a section of the spinal cord (hematoxylin and eosin preparation). Hold the section to the light and view it with a hand magnifier. Observe the general outline of the section. Note that the white substance of the cord surrounds a somewhat darker, H-shaped portion, the gray matter. The upper limbs (dorsal horns) of the gray matter are considerably narrower than the lower limbs (ventral horns).

Examine the ventral horns with the low power and find a number of large, deeply stained cells having an irregular outline and large, vesicular nuclei—the motor cells of the ventral horn of the spinal cord. Select a few of these cells, in which the outline of the nucleus is clearly discernible and examine with the high power. Note the general form shown by the outline of the cells. Is the nucleus densely chromatic or vesicular? Observe the arrangement of the chromatin material in the nucleus. Identify the nucleolus. Is there more than one nucleolus present? Note the character of the cytoplasm. Is it granular? What evidence is there of processes (dendrites and axon) extending from the cytoplasm of the cell? To what class of nerve cells do these cells belong?

Draw several of these motor cells of the ventral horn, showing their form and structure as you observe them in the section.

With the high power examine a smear preparation made from the freshly obtained spinal cord of one of the larger animals, which has been stained with erythrosin and toluidin blue or by the pyridine silver method. Observe the general structure of the cell. The processes of these cells can be followed for a considerable distance from the cell body. The dendrites are to be identified by their gradually diminishing diameter and their method of branching; the axons by their origin from the granular protoplasm of the axon hillock, and their constant diameter. Do all axons arise from an axon hillock? Do you find any indications of the presence of neurofibrillae in these cells?

Draw several of the cells observed in the preparation, showing their structure as indicated above.

Examine a section of the spinal cord stained by the reduced silver method (the methods of Rogers or Davenport are recommended). Note the presence and arrangement of the neurofibrillae. Draw.

Using the oil-immersion objective examine a similar section stained with toluidin blue or carbolthionin. Note: the general structure of the nerve cells; the large, angular masses of deeply stained material (Nissl bodies) present in the cytoplasm; the rodlike form which these bodies assume as they extend into the dendrites. Are the Nissl bodies present in the axon hillock or axon?

Draw several of the cells showing the form and distribution of the Nissl bodies.

NERVE FIBERS. With the high power examine preparations of nerve fibers which have been teased apart and treated with osmic acid. The wrinkled appearance of the fibers is due to shrinkage and should be disregarded. Note: the light, central core of the fiber (axis cylinder); the portion on either side of the axis cylinder which is stained a deep black (myelin sheath); the constrictions by which the myelin sheath is interrupted at more or less regular intervals along the course of the fiber (nodes of Ranvier). Observe the difference in the diameters of the axis cylinders in different fibers; also variations in the thickness of the myelin sheath. In what fibers is the thickness of the myelin sheath greatest as seen in relation to the diameter of the axis cylinder? Why is the myelin sheath blackened by osmic acid? Is there any change in the diameter of the axis cylinder as it passes through the nodes of Ranvier? Where some of the nerve fibers are broken and twisted, the neurilemma can be seen as a delicate, unstained membrane passing from one segment of the broken fiber to the other.

With the high power, examine nerve fibers which have been sectioned longitudinally and treated with osmic acid. Follow the outline for the general study of the section. Using the oil-immersion objective observe the light, obliquely directed lines in the myelin sheath (incisures of Schmidt-Lantermann).

Draw: including the structures observed in one, or both, of the preparations studied.

Examine with the high power, a preparation of nerve fibers sectioned longitudinally and stained with Mallory's phosphotungstic acid hematoxylin. Note: the axis cylinders, having the appearance of a light purple, ribbonlike band in the middle of each fiber; the myelin sheath, seen as delicate, reddish lines which form the neurokeratin network about the axis cylinder. The meshes of this network are filled, in the fresh condition, with the myelin substance. Observe the neurilemma (sheath of Schwann) which is seen as a fine, blue line on the surface of the fiber. Here and there, the neurilemma is raised from the surface to provide space for the neurilemmal nuclei, which are stained a deep red.

Draw: showing the structures observed in the section.

Examine a cross section of a nerve trunk (preferably of the sciatic nerve) with the low power. Note the appearance of the section as a whole. It will be seen to consist of a number of well-defined bundles of nerve fibers (funiculi) *bound together by loosely interwoven connective* tissue (epineurium). The connective tissue of the epineurium is condensed about each funiculus to form a densely compacted fibrous sheath (perineurium). Extensions of the perineurium into the funiculi form septa (endoneurium) by which *the nerve fibers are separated into* groups. Delicate fibers of the endoneurium extend between and around the individual nerve fibers. In some instances the funiculi are divided into two or more parts by partitionlike extensions of the perineurium. What does this indicate?

Draw: showing the appearance and structure of a nerve trunk as seen in the section.

Examine a single funiculus with the high power. Note: the loose arrangement of the fibers of the surrounding epineurium; the more compact arrangement of the connective tissue which forms the perineurium; the extensions of connective tissue from the perineurium into the funiculus to form the endoneurium; the endoneurial septa which separate the nerve fibers into groups; the more delicate extensions of the endoneurium between the nerve fibers. By using the oil-immersion objective, the lamellated structure of the perineurium may be observed.

Owing to the wavy course of the fibers in the funiculus, some of the fibers are cut obliquely, while others are cut transversely. Using the oil-immersion objective, examine some of the fibers which have been cut transversely. Note the axis cylinder appearing at the center of a circle, the circumference of which is outlined by the neurilemma. Observe the somewhat granular appearance of the axis cylinder. What appear as granules are the cut ends of the neurofibrillae. The space between the axis cylinder and the neurilemma is occupied by the myelin sheath, the substance of which has been removed by the solvent action of the reagents employed in the preparation of the section. Are any traces of the neurokeratin framework visible?

Examine a section of the spinal cord, using the oil-immersion objective. Note the numerous nuclei of the neuroglial cells in the white and gray matter of the cord. Special staining methods are necessary to bring out all the details of structure in these cells, but much can be learned from a study of their nuclei as they appear in ordinary preparations of the central nervous system. Note that nucleoli are not present in these nuclei, one of the characteristics by which they can be distinguished from the nuclei of nerve cells.

Observe: large, oval and somewhat irregular nuclei, containing only a few scattered granules of chromatin—nuclei of astrocytes; somewhat smaller nuclei, round or nearly so in outline, the chromatin granules *being* larger and more numerous than in the nuclei of astrocytes—the nuclei of oligodendroglial cells; nuclei which are much smaller and which show a greater irregularity of form than those of the preceding cells, being frequently elongated and bent, the chromatin granules being large and abundant—nuclei of microglia cells. Note that these nuclei are considerably darker than those of the other types. *Which type of nucleus is most numerous in relation to the nerve* fibers in the white matter? Which type is most commonly seen about the blood vessels? Which type appears most frequently in association with the nerve cells in the gray matter.

Draw a number of these nuclei showing (1) their typical appearance; (2) their relations with the structures named above.

NERVE ENDINGS. Meissner's corpuscles and Pacinian corpuscles can be readily identified in the hematoxylin and eosin stained structures in which they occur. For the observation of end bulbs, muscle spindles and the endings of motor nerves, material prepared by one of the reduced silver methods must be used.

MEISSNER'S CORPUSCLES. With the high power, examine sections of the skin from the volar surface of the tip of the finger. Meissner's corpuscles will be found in the connective tissue of the larger dermal papillae. What is the shape of the corpuscle? Note: the connective tissue capsule by which the corpuscle is enveloped; its striated appearance, due to extensions of the capsule into the corpuscles, and the horizontal arrangement of the wedge-shaped (tactile plates) which they support. In sections which have been prepared by special methods, the spiral course of the nerve fibers can be followed in the corpuscle as they wind about between the tactile plates. A number of swellings (varicosities) can be seen along the course of the nerves. Branches of the nerves, ending between and upon the tactile plates can be made out in silver preparations. To what type of stimuli do these corpuscles react?

Draw one or two Meissner's corpuscles, showing their appearance as observed.

PACINIAN CORPUSCLES. With the low power, examine a section of the skin from the palm of the hand which includes the deeper portions of the subcutaneous tissue. Find one or two Pacinian corpuscles which, in sections of this kind, are usually cut transversely or diagonally. Longitudinal sections in which the core appears are rarely seen in ordinary preparations. Larger Pacinian corpuscles may be found in sections of the mesenteric lymph glands, their location being in the vicinity of the hilum.

After you have found the corpuscles examine them with the high power. Note: the capsule which consists of a thin, external layer of connective tissue; the lamellae, which appear as a series of concentric circles about the central core; the central core, consisting of a number of neuroepithelial cells on the border of a central mass of granular protoplasm.

Examine a few of the lamellae with the oil-immersion objective. Note that they consist of thin layers of connective tissue between which are fluid spaces, lined by a tissue which bears a close resemblance to endothelium. To what type of stimuli do the corpuscles react?

Draw: showing the structure of a Pacinian corpuscle as seen in the section.

As a rule, sections of end bulbs are unsatisfactory for general laboratory study. The majority of the sections fail to pass through the entering nerves, so that only the capsule and a few of the coiled fibers which it contains are visible. End bulbs may be seen in the subepithelial tissue in sections of the glans penis which have been stained by the silver method. These are the genital corpuscles which are larger than, but otherwise similar to the end bulbs of Krause.

SENSORY NERVE ENDINGS IN MUSCLE (MUSCLE SPINDLES). These may be observed in cross sections of the leg muscles of one of the lower animals. In the perimysium, note a small area encircled by a ring of condensed connective tissue (capsule), in which a few, small, striated muscle fibers are enclosed, the structure forming a muscle spindle.

For the manner in which the terminal branches of the nerves end in relation to the muscle fibers in the spindle, a muscle spindle should *be dissected out and separated from the surrounding muscle fibers by* teasing the fibers apart with needles. The preparation is then treated by the Cajal or Golgi method. Note that the terminal fibers of the nerve end in relation to the muscle fibers in the spindle in one of two ways: by winding around the fiber in a ringlike or spiral fashion (annulospiral ending), or by breaking up into a number of branching fibers which end in platelike expansions on the surface of the muscle fiber.

Draw: showing the appearance of a muscle spindle as seen in cross section; the *manner in which the terminal branches of the nerve end in relation to the muscle* fibers in the spindle.

MOTOR NERVE ENDINGS IN STRIATED MUSCLE. Examine a preparation of an intercostal muscle from one of the smaller animals, in which the course of the nerve to the muscle has been traced by dissection; the fibers having been teased apart with needles and the preparation treated by the method of Cajal or Golgi. Note: the division of the nerve into its terminal branches; the small, oval plate of modified sarcoplasm (sole plate) *in which the terminal fibers of the nerve* (end arborization) end. The terminal fibers and the sole plate, together, form a motor end plate.

In a fiber, where the motor end plate can be seen in profile, note the manner in which it forms an elevation on the surface of the muscle fiber.

Draw showing the division of a motor nerve into its terminal branches, and the manner in which the branches end in relation to the muscle fiber.

STUDY OF THE VASCULAR ORGANS

ELASTIC ARTERIES—AORTA. Examine the wall of the aorta (hematoxylin and eosin preparation) with the low power. Identify the intima, media and adventitia. Note the relative thickness of these three layers.

Examine a portion of the aortic wall with the high power. Note: the intima, consisting of a layer of endothelial cells which rest on a thick layer of subendothelial connective tissue beneath which is a layer of elastic tissue; the media, consisting of smooth muscle fibers arranged in layerlike bundles, which give it a lamellated appearance, and the connective tissue septa which extend between the muscle bundles; the elastic tissue, in the form of fenestrated membranes, which are to be seen as light, wavy lines in the intima and in the connective tissue between the muscle bundles; the adventitia, a relatively thin layer of fibrous tissue lying on the external surface of the media. What is the direction of the fibers in the intima? Identify and observe the vasa vasorum by means of which blood is supplied to the aortic wall.

Examine a portion of the wall of the aorta, prepared with Verhoeff's stain, with the high power. Note: the delicate elastic fibers in the portion of the intima just beneath the endothelium; the fenestrated membranes in the deeper portions of the intima; the strongly developed fenestrated membranes between the muscle layers in the media; the delicate elastic fibers which pass from one fenestrated membrane to another (radial fibers). Can an elastica interna be readily identified in the aorta? Does muscular tissue, or elastic tissue, predominate? Which of these tissues predominates in the wall of a medium-sized artery?

Draw: showing the arrangement of the muscle and elastic fibers in the wall of the aorta.

MUSCULAR ARTERIES—MEDIUM-SIZED ARTERIES. Examine the section of a medium-sized artery (hematoxylin and eosin preparation) with the low power. Note the full, open appearance of the artery. Identify the intima, media and adventitia.

Change to high power and examine a portion of the wall of the artery. Locate the intima and identify the nuclei of the cells lining the vessel. Can you see the cytoplasm of these cells? What are these cells and what is their shape? The intermediate layer of the intima consists of what kind of tissue? Is this layer relatively thick or thin. Identify the internal elastic membrane. Can you find an area where this membrane splits to form a double membrane? In the smaller muscular arteries what changes, if any, take place in the appearance of these three layers?

Examine the media. How does the thickness of this layer compare with the thickness of the intima? Compare the relative thickness of the media of a muscular artery with that of an elastic artery. How are the muscle fibers of this layer arranged? In one of the larger muscular arteries observe the elastic fibers which appear as highly refractive, wavy lines. Can you make out any definite arrangement of these elastic fibers? Compare their arrangement in this artery with one of the smaller muscular arteries. Is there any connective tissue present between the muscle bundles? If so, what is its relation to the elastic fibers?

Locate the adventitia and compare the thickness of this layer with that of the media. This layer is made up of what kind of tissue? Can you verify the statement in the text that the inner fibers of this layer are directed longitudinally? How does the outer layer of the adventitia differ from this, both in arrangement and compactness? Can you identify any smooth muscle fibers in the adventitia?

With the high power, examine a section of a large and a small muscular artery stained with Verhof's elastic tissue stain. Observe the amount and distribution of the elastic fibers in the three layers of these two muscular arteries. Compare them with the aorta.

ARTERIOLES. Examine a "typical" arteriole and note the relative thickness of the layers. Examine each layer, following the procedure given for muscular arteries.

VEINS. With the low power examine a section of a large vein stained with hematoxylin and eosin. Note the more or less collapsed condition of the vein which is due to the relative thinness of its wall. Identify the intima, media, and adventitial layers.

With the high power examine a portion of the wall of this vessel. Notice the relative thickness of the three layers. Compare the veins, layer for layer, with an artery of comparable size. Can you distinguish a well-defined internal elastic membrane in the vein? Is there any change in the relative amounts of muscle, or collagenous and elastic fibers in veins as compared to arteries of approximately the same size?

Examine a section of a vein stained with Verhoeff's elastic stain. Compare the amount and distribution of the elastic tissue in the wall of the veins with that in the wall of the artery.

MEDIUM-SIZED VEINS. Notice the thickness of the intima. Is there an internal elastic membrane? Is it well-developed? Observe the relative thickness of the media. How are the muscle fibers arranged in this layer? Examine the adventitia. How does this layer compare in thickness with the media? Notice that the adventitia is composed of loosely interwoven collagenous fibers. Can you identify any smooth muscle fibers in the adventitia?

VENULES. Examine a medium-sized venule with low and then high power. Is there an internal elastic membrane present? Note the thickness of the media. How are the muscle fibers of the media arranged? Observe the adventitia. Is it a relatively thick or thin layer? How are the fibers of the adventitia arranged? Are there any elastic fibers present in this layer?

Draw: Make drawings of narrow wedge-shaped sections through the various vessels studied. Keep the relative thickness of the layers in correct proportion so that they may be compared and their differences seen.

VALVES OF VEINS. Examine a longitudinal section of a vein showing a valve. Note the way the valves are attached to the wall of the vein and how they are directed. Do all veins have valves? What layer, or layers, of the vein contribute to the formation of the valve? Are there elastic fibers present in the connective tissue of the valve? Is it distributed evenly throughout the connective tissue or is it more compactly arranged on one side of the valve than on the other? If so, on which side?

THE HEART. Examine the heart of an animal which has been dissected to show its internal structure. Observe the thinness of the walls of the atria: the openings through which the large vessels (venae cavae and coronary sinus) communicate with the right atrium; the openings of the pulmonary veins into the left atrium; the atrioventricular openings through which blood passes from the atria into the ventricles; the atrioventricular valves arranged about these openings. The valve on the right side of the heart consists of three flaps, that on the left side, of two flaps. Note the chorda tendineae by means of which the borders of the flaps are attached to the papillary muscles; the ridgelike columns of muscle tissue (columnae carnae) on the inner walls of the ventricles. Identify the pulmonary artery which leads from the right ventricle, and the aorta which leads from the left ventricle, noting the semilunar valves formed by three pocketlike cusps, located at the root of each of these vessels. Observe the thin, glistening membrane (endocardium) which forms the lining of the heart; also the fibrous layer (epicardium) which lies on the external surface.

Examine with the low power a section which includes the entire thickness of the ventricular wall of the heart. Use the high power whenever necessary for verifying details of structure. Note: that the epicardium consists of a layer of thin, flattened cells with bulging nuclei (mesothelium); the thin substratum of connective tissue on which the mesothelial layer rests. The mesothelium and its subjacent connective tissue, are the visceral portion of the pericardium, which is reflected onto the surface of the heart. It can be seen best where it has been raised slightly from the underlying tissue. Note that the epicardium increases in thickness as it passes over the places where blood vessels are located.

The muscular layer or myocardium consists of cardiac fibers arranged in partially formed bundles. The irregular disposition of these bundles is indicated by the directions in which the fibers are cut (longitudinal, oblique and transverse). Observe the manner in which the muscle bundles are partially separated by thin septa of connective tissue, which form the endomysium.

The endocardium consists of a layer of flattened endothelial cells, which rest on a thin layer of connective tissue. By following the septa of the endomysium, it will be noted that the connective tissue which forms the framework of the heart, is continuous from the epicardium to the endocardium.

Draw, showing the structure of the heart wall.

THE HEART VALVES. THE ATRIOVENTRICULAR VALVE. Examine a longitudinal section of the valve with the low power. Note: the portion of the myocardium to which the valve is attached; a mass of fibrous tissue, so compact that it has almost the appearance of cartilage, can be seen at the root of the valve (annulus fibrosus): the endothelial layer which covers both the atrial and ventricular surfaces of the valve; the closely interwoven collagenous and elastic fibers, between the folds of the endothelium, by which the valve is supported. Note that the connective tissue between the folds is continued into the valve from the annulus. Small bundles of cardiac fibers extend from the myocardium into the root of the valve. Where the section passes through the chorda tendineae, they will be seen to consist of collagenous and elastic fibers surrounded by endothelium, both being extensions of the tissues of the valves.

THE SEMILUNAR VALVES. Examine a longitudinal section of a valve with the low power. Note that its structure is nearly similar to that of an atrioventricular valve, in that it consists of two opposed layers of endothelium supported by a compact mass of fibroelastic tissue. A small amount of smooth muscle may be seen at the root of the valve. What is the direction of these muscle fibers? This probably acts as a sphincter to aid in rendering the valve more tense. Note that the wall of the aorta (or pulmonary artery) is adjacent to the valve. In sections which pass through the mid-portion of the valve, a considerable accumulation of connective tissue is to be observed at its free border. This tissue is densely compacted, and forms the enlargement known as the nodule of Arantius.

ATRIOVENTRICULAR BUNDLE OF HIS (IMPULSE-CONDUCTING SYSTEM). Examine, with the high power, a longitudinal section of the Bundle of His. Material for this study is most readily obtained from the heart of a young calf. Observe a narrow area on the border of the section which stands out *distinctly from the myocardium. Note, in this portion of the* section, a number of lightly stained muscle fibers, conspicuously larger than the fibers of the myocardium; their very faint cross striations; numerous small nuclei, observing their tendency to present a double appearance and that they are more superficially placed than the nuclei of the myocardial fibers. Note, also, the dark bands which cross the fibers at more or less regular intervals, giving them the appearance of being *divided into short, thick segments. Observe the connective tissue* sheath by which the neuromuscular fibers are enclosed and which separates the Bundle of His from the myocardium. The muscle fibers in the Bundle are separated by connective tissue septa which are continuous with the sheath. Note the bundles of nerve fibers in the septa.

Examine, as above, a transverse section of the Bundle of His. Note: the clearly defined sheath by which each fiber in the Bundle is enclosed; the myofibrillae, gathered into irregular groups about the periphery of the fiber; the clear sarcoplasm with which the fibers are filled. The nuclei, which are more superficially located than in the myocardial fibers, are embedded in the sarcoplasm. Note the disposition of the connective tissue between the neuromuscular fibers in which bundles of nerve fibers are to be observed as in the longitudinal section.

Draw: showing the structure of the Bundle of His as observed in longitudinal section; as observed in cross section.

THE LYMPH VESSELS. Lymph vessels may be observed in sections from the mesentery in which blood vessels and a lymph gland are present.

Find one or more lymph vessels and examine with the high power. Note: the layer of endothelium by which the vessel is lined. The cells forming this layer will be identified, principally, by their bulging nuclei. Observe that the endothelium lies immediately on the muscular layer. Note the thin layer of circularly arranged smooth muscle fibers, the media. A layer of obliquely directed muscle fibers is to be observed external to the layer of circular muscle fibers. Valves are to be seen in some of the vessels, their structure being similar to the valves described for the veins. The adventitia is formed by an external coat of connective tissue. Compare the coats in the wall of a lymph vessel with those in the wall of a blood vessel.

THE THORACIC DUCT. Examine a section of the thoracic duct, first *with the low power for its general appearance, then with the high power* for details of structure.

Note: the intima, consisting of endothelial cells and a subendothelial layer of collagenous and elastic fibers. The arrangement of the elastic fibers at the junction of the intima and media, suggest an elastica interna. Observe the arrangement of the smooth muscles in the media. In the lower portion of the duct the inner layer of muscles is directed longitudinally, the fibers of the outer layer are directed obliquely. In the higher levels the longitudinal fibers disappear and the inner layer of oblique fibers becomes circularly arranged. Obliquely directed bundles of muscle fibers are also present in the adventitia. Note that the muscle bundles are somewhat widely separated by connective tissue septa, a characteristic feature of the thoracic duct.

Draw: one or two lymph vessels from a section of the mesentery, including a study of the valves; a section of the thoracic duct.

STUDY OF THE LYMPHOID ORGANS

The Lymph Gland

Examine a section of a lymph gland with the low power. Observe the capsule which consists of closely interwoven collagenous and elastic fibers; also the trabeculae which are to be identified as extensions of the connective tissue of the capsule into the parenchyma of the gland. What direction do the trabeculae take in relation to the capsule? Are the trabeculae solid and continuous? Compare with the trabeculae in the spleen. Note the two areas into which the parenchyma is divided: the cortex, which is the peripheral area in which the lymphocytes are aggregated in the form of nodules surrounded by diffuse lymphoid tissue; the medulla, the area partially enclosed by the cortex in which the lymphoid tissue is in the form of branching and anastomosing cords. Observe the nodules in the cortex. Do all of the nodules show germinal centers? How can you account for this? Note that the areas between the nodules are filled with diffuse lymphoid tissue and then observe how this diffuse tissue extends into the medulla to form the cords. Note that these cords branch, the branches anastomosing with other cords or branches to enclose spaces between them which are free, or nearly free, from lymphocytes. What are these spaces called?

Identify the peripheral sinus between the cortex and the capsule. Follow the spaces on both sides of the trabeculae. These are lymph channels (sinuses) which continue from the peripheral sinus into the substance of the gland. Can you find any communications between these sinuses and the lymph spaces in the medulla? Try to locate afferent lymph vessels that are penetrating the capsule to communicate with the peripheral sinus. What is the course of the lymph through a lymph gland. Note the large blood vessels in the region of the hilum; the blood vessels in the trabeculae and capsule; the arteries in relation to the lymph nodules. What does this observation reveal regarding the blood supply of a lymph gland? Make a diagram to represent the course of the lymph and its relation to the blood vascular circulation.

Examine the following with the high power: the germinal center of a lymph nodule. Identify the small, medium-sized and large lymphocytes. In what part of the nodule are small lymphocytes most abundant? In what cells are mitotic figures to be observed? What does this indicate regarding the function of the germinal centers? Identify the macrophages (the lymphoblasts of some authors) which are irregularly shaped cells, somewhat larger than the large lymphocytes. Observe their basophilic cytoplasm and large vesicular nuclei.

In the lymph spaces in the medulla note that these spaces are not separated from the lymphoid tissue by a layer of endothelium and therefore are not to be regarded as true vascular spaces. Portions of the reticulum can be seen in these spaces, the meshes being exceptionally wide. How does this explain the fact that the spaces are free from lymphocytes? Reticulocytes can be identified in these spaces by their attachment to the reticulum. What other types of cells can be observed?

Observe the delicate fibers which extend across the sinuses from the capsule and trabeculae to the parenchyma. What does this indicate regarding the relation of these structures to the reticular framework of a lymph gland? How is this observation supported by a study of the section of a lymph gland from which the lymphocytes have been removed (see study of reticular connective tissue)? What kinds of cells are to be observed in the sinuses? Are other types of cells to be found in lymphoid tissue? How is their presence to be explained?

For a more accurate determination of the types of cells to be found in a lymph gland, thin sections stained with Wright's, Giemsa's, or the azure-eosin hematoxylin stains should be studied with the oil-immersion objective.

Draw: (1) the germinal center of a lymph nodule; (2) one of the larger lymph spaces in the medulla; (3) a portion of the peripheral sinus.

THE HEMOLYMPH GLAND

Examine a section of a hemolymph gland with the low power, using the high power for verifying details. Note: the close resemblance of a hemolymph gland to a lymph gland; the irregular distribution of the lymphoid tissue in the cortex. Observe the presence of nodules. Are they provided with germinal centers? Note the branching and anastomosing cords of lymphoid tissue in the medulla; also the large, sinus-like spaces between the cords. The peripheral sinus, and the spaces between the cords in the medulla, are filled with red corpuscles. Record the ways in which hemolymph glands differ from lymph glands.

THE SPLEEN

Examine a section of the spleen with the low power. Observe the capsule. What kinds of tissue form the capsule? Which type of tissue predominates? What is its distribution? Observe the trabeculae. How do they differ from the trabeculae studied in the lymph node. Identify the network of reticular fibers. Note the meshlike arrangement of these fibers. What cells are caught and held in these meshes? Examine a splenic nodule (Malpighian corpuscle) which consists of nodular masses of lymphoid tissue which have been formed about the branches of the splenic artery. One and sometimes two branches of the central artery can be seen in each nodule. Note the position of the central artery in the splenic nodule. Observe the cordlike arrangement of the cells of the splenic pulp between the sinusoids. Is it possible to identify the cells forming the walls of the sinusoids?

For the identification of the different types of cells use a thin section of spleen that has been stained with one of the blood stains mentioned in the study of the lymph gland.

Using the oil-immersion objective identify the following types of cells which are normally present in splenic pulp: red blood corpuscles, usually the most abundant of the cellular elements of the pulp; lymphocytes, found most abundantly in and around the splenic nodules (their number in the red pulp is relatively small); monocytes, cells resembling lymphocytes but considerably larger. These cells occur in large numbers and, except for the red corpuscles, are the most abundant of the cellular elements of the pulp. In the older literature they were called splenic cells or splenocytes, and were regarded as being peculiar to the spleen. Find cells of this type which have fragments of ingested red corpuscles in their cytoplasm. Note, also, the different forms of granulocytes which have entered the spleen in the blood stream.

BLOOD SUPPLY OF THE SPLEEN. Examine a section of an injected spleen with the low power. Note: the large vessels in the region of the hilum—branches of the splenic artery. Trace these branches as they pass into the trabeculae to become the trabecular arteries. Identify the central arteries in the splenic nodules. Observe the brushlike penicillus in the red pulp. What are the three successive divisions of the pencillus? Can you identify these subdivisions?

The injected material, like the blood, passes from the sinusoidal capillaries into the pulp and has the appearance of being diffused through the substance of the spleen. The portion of the spleen, which has been colored in this manner indicates the red pulp. In contrast to this area, the splenic nodules appear an almost clear white and show as the white pulp.

THE THYMUS

Examine a section of the thymus with the low power. Observe the division of the gland into lobules. Note that there is a confluence of the lighter, medullary portion of several of the subdivisions or primary lobules, to form a larger division, or secondary lobule. Note, also, that the subdivisions of the gland are incomplete. Examine the capsule formed by an external layer of fibroelastic tissue. Follow the septa as they extend from the capsule between the subdivisions of the gland, thus forming the boundaries of the lobules. Observe the cortex, the dark peripheral area containing numerous, closely packed, small cells (thymocytes) which give the cortex the appearance of lymphoid tissue. Observe the medulla which is seen as much lighter areas enclosed by the cortex. Note that the medullary portions of the lobules are joined together; the lobules being separated by connective tissue extensions of the capsules between their cortical portions. Identify the thymic corpuscles (Hassall's corpuscles), which are highly refractive bodies with a marked acidophilic reaction, their cellular elements having a concentric arrangement. Can thymic corpuscles be found in the cortex?

Draw: showing the structural appearance of the thymus as seen in the section.

Examine a single lobule under high power. Observe the closely packed thymocytes in the cortex, noting their close resemblance to lymphocytes. Locate and observe the blood vessels in the connective tissue between the lobules. Note the stellate form of the cells of the reticulum which constitutes the supporting structure of the gland. Identify the thymic corpuscles, noting that they consist of a central cell, or amorphous mass of hyaline material, surrounded by one or more layers (according to the size of the corpuscle) of enlarged, concentrically arranged cells.

Draw: (1) A part of a lobule showing its structural details. (2) One or two corpuscles, enlarged, showing their structure and characteristic appearance.

The Tonsils

THE PALATINE TONSIL

Examine a section of a palatine tonsil with the low power. What type of epithelium covers the superficial surface of this tonsil? Follow the epithelium into the crypts. Does the type of epithelium change in the crypts? Observe the numerous nodules with large germinal centers beneath the epithelium and about the crypts; the diffuse lymphoid tissue by which the nodules are surrounded. Locate areas where the masses of lymphocytes have invaded the epithelium on the surface of the tonsil and in the crypts. Note that the cells of the epithelial tissue are hidden because of the large number of these invading lymphocytes. Can lymphocytes be identified on the surface of the tonsil? Are any present in the crypts?

Identify the capsule of the tonsil. This capsule is composed of what kinds of tissue? Are there any trabeculae present in this tonsillar tissue?

If present compare them with the trabeculae in the lymph gland and spleen. Is there a peripheral sinus? Identify the mucous secreting glands which lie in the connective tissue outside the capsule. Wherever possible follow the ducts of these glands to their junction with the deep portions of the crypts. Identify the muscular tissue which is located subjacent to the tonsil. *What type of muscle tissue is it?*

THE PHARYNGEAL TONSIL

Examine the section with the low power, noting that the tonsil consists of a single row of relatively small lymph nodules surrounded by diffuse lymphoid tissue. If the tissue is in the hypertrophied (adenoid) condition, the number of the nodules will be increased and they may be arranged in two or more superimposed layers. Note the type of epithelium by which the tonsil is covered. Normally the epithelium is of what type? Under certain conditions this epithelium may be replaced by what other type of epithelium? Verify the statement that in such abnormal conditions the original epithelium still persists in the crypts. Note the thin layer of connective tissue which is interposed between the lymphoid tissue of the tonsil and the bone.

THE LINGUAL TONSIL

Examine a section of a lingual tonsil with the low power. Note: the type of epithelium which lies upon the surface of the tonsil; the tonsillar crypts, about which the nodules are clustered. The nodules in the lingual tonsil are characterized by their large size and by the constancy of their germinal centers. Observe the dense arrangement of collagenous and elastic fibers about the deep surface of the tonsil. This does not form a true capsule, although it is so considered by some. Mucus-secreting glands can be seen in the surrounding tissue; their ducts should be traced to the crypts, into which they open. Can any mucoid material be seen in the crypts?

THE TUBAL TONSIL

With the low power examine a section which includes the opening of the Eustachian tube into the pharynx. Note the masses of diffuse lymphoid tissue clustered about the opening of the tube. Are any nodules present? These masses of lymphoid tissue are continuous with the pharyngeal tonsils. Owing to their position about the Eustachian tube, they are sometimes called the tubal tonsils.

WALDEYER'S PHARYNGEAL RING

The phagocytic cells produced by the activity of the tonsils, exist for the removal of organisms and particulate matter which lodge on the mucous membranes of the fauces, the oral cavity and the upper respiratory passages. Therefore, the tonsils are to be regarded as important protective structures. This is also indicated by their arrangement, which forms an incomplete ring about the respiratory and oral openings. This ring consists of the pharyngeal tonsils above, the palatine *tonsils on* either side, and the lingual tonsil below, and is known as the pharyngeal lymphoid ring of Waldeyer.

BLOOD AND NERVE SUPPLY OF THE TONSILS

The vessels which supply the tonsils with blood, enter the capsular tissue from below and at various points on the sides. These vessels pass into the tonsil and into the trabecular tissue, which they leave to enter the nodules in the manner already described for the lymph glands and spleen.

The nerves are branches from the sympathetic system, and are distributed to the walls of the blood vessels. Some sensory fibers are also present.

METHOD OF IDENTIFICATION OF LYMPHOID ORGANS

Given an unknown section for identification. If the tissue is predominately lymphoid tissue it is undoubtedly one of the lymphoid organs. This limits the material to one of the following: lymph gland, spleen, tonsils or thymus.

Examine the periphery of the section quickly with low power to *see if any surface is covered by an epithelium. If any epithelium is* present it must be one of the tonsils. Identify the epithelium in the bases of the crypts. If it is a pseudostratified columnar it is pharyngeal tonsil (Note: Do not depend on the type of epithelium at the surface for this identification, because under certain conditions, mentioned in the text, the pseudostratified epithelium in this more exposed region can become stratified squamous type).

If the epithelium in the base of the crypts is stratified squamous it is either palatine or lingual tonsil. Observe the capsule. If it is a thick, well-defined layer, it is probably palatine tonsil. However, check the crypts and distribution of the lymph nodules. In palatine tonsils the crypts are longer and the lymph nodules are numerous and are located both beneath the surface epithelium and about the crypts. In lingual tonsil the crypts are pitlike invaginations and the nodules are clustered about the crypts only.

If there is no epithelium present, the section is: lymph gland, spleen or thymus. Next examine the section to see if it appears lobulated. If it is, *it probably is thymus. Check for the following: poorly defined* capsule with septa extending between the lobules; an outer, relatively even thickness of more deeply staining tissue around each lobule, enclosing a lightly staining central portion. The presence of Hassall's corpuscles in the medulla. If there is no indication of lobulation it is undoubtedly lymph gland or spleen.

Positive identification of lymph gland depends on the following: definite connective tissue capsule; peripheral sinus; cortex and medulla; lymph nodules with germinal centers in cortex.

Positive identification of spleen may be made if section shows: areas of red and white pulp; lymph nodules with central artery; discontinuous trabeculae in parenchyma of organ.

STUDY OF THE DIGESTIVE SYSTEM

THE LIP

Hold a section of the lip to the light and examine with a hand magnifier. Observe the following: the outer or cutaneous surface which may be recognized by the presence of hair follicles and other structures characteristic of the skin; the inner or oral surface which may be distinguished by the thickness of its epithelium and the presence of labial glands; the border, noting the increasing thickness of the epithelium as it passes from the cutaneous to the mucous surface; bundles of transversely cut striated muscle in the middle of the section.

Examine the section with the low power observing:

THE CUTANEOUS SURFACE. Note: the thin layer of stratified squamous epithelium (epidermis); the layer of dense areolar tissue or corium on which the epithelium rests (derma); the low, connective tissue papillae extending into the deep surface of the epithelium. Identify the hair follicles—tubular invaginations of the epithelium—noting the depth to which they extend into the corium. Observe the sebaceous glands. What is their shape? Do these glands have a lumen? Do they have ducts? How do they secrete? Where does this secretion empty? Identify the sweat glands. They are long, slender, tubular glands, the coiled secreting portions of which are located in the deeper portions of the corium. Segments of the ducts of these glands may be found in the corium between the hair follicles The coiled portions of some of the sweat glands may also be found in the loose subcutaneous tissue.

THE BORDER. What change takes place in the epithelium as it passes from the cutaneous surface to the mucous surface of the border? If the section is through the lip of an infant, identify the sucking disc. On what part of the lip is it located? In what respects does the epithelium of the sucking disc differ from that of the other portions of the lip?

THE ORAL SURFACE. Note the type of epithelium by which this surface is covered. How does it compare in respect to thickness with that on the cutaneous surface? Observe the loose arrangement of the submucous connective tissue and the labial glands which are embedded in it. If possible find ducts from these glands which open to the surface of the epithelium. Are any traces of a mucoid substance to be seen in the ducts? How are these glands to be identified as mucus-secreting structures. What evidence may be observed that the mucous membrane is more sensitive than the integument?

THE MUSCULAR STRUCTURES IN THE LIP. Note the bundles of striated muscle fibers which are located between the subcutaneous and submucous tissues. How are the fibers cut in the section? How are they to be recognized as striated fibers? To what muscle do they belong? Note the septa of connective tissue by which the muscle bundles are separated, observing that they extend from the submucous to the subcutaneous tissues. Identify the branches of the labial artery which appear in the section.

Draw the section of the lip showing the histological elements of which it is composed.

THE TOOTH

THE ADULT TOOTH. Examine a ground section of a tooth with the low power, using the higher powers to verify details of structure. Observe: the general form of the tooth, noting that this form is maintained by the dentine upon which are laid down the enamel in the crown and the cementum in the root. Identify the pulp cavity, in which remains of the odontoblasts and dental pulp may be seen. Examine the root canal, which may be traced from the pulp cavity to the apical foramen at the tip of the root. What does it contain? Locate, and with the high power observe the enamel rods, noting their arrangement in bundles and the different planes in which the bundles lie. Identify the lines of Retzius. They are dark lines which cross the rods transversely and indicate successive periods in the growth of the enamel. Identify the dentinal tubules: fine, dark, S-shaped lines which pass through the dentine from the pulp cavity to the dentoenamel junction. Note the manner in which they branch in the dentine immediately beneath the enamel layer. Locate the granular area of Tomes, the area immediately beneath the cementum which may be recognized by the granular appearance of the dentine and the presence of numerous, irregular, dark areas, indicating spaces in the dentine. Observe the cementum, the external layer, resembling the structure of bone in its general appearance. Note its lamellae and the presence of lacunae and canaliculi. Does it have Haversian systems?

Draw: showing the structural appearance of a ground section of a tooth.

RELATION OF THE TOOTH TO THE ALVEOLUS. With the low power examine a section which includes a fully developed tooth and the adjacent portions of the jaw. Before the section can be cut the process of decalcifying the bone frequently results in the distortion of the softer tissue, hence sections of this kind are more useful for the study of relationships than for histological detail.

Observe: the alveolus or pitlike excavation in the bone which is occupied by the root of the tooth; the oral epithelium which, together with the substratum of connective tissue on which it rests, forms the gum (gingiva). Note that the epithelium dips downward before coming in contact with the sides of the tooth, forming a furrow between the gum and the surface of the tooth. What is this furrow called? Identify the crown, which is that portion of the tooth which rises above the level of the gum; the root, which occupies the alveolus; the neck or the slightly constricted portion at the point where the cementum and enamel meet, indicating the junction of the root and crown; the periodontal membrane, formed by the connective tissue which occupies the space between the root and the alveolar wall; the pulp cavity, noting the odontoblasts which line the wall of the cavity, and the dental pulp by which it is filled; the root canal, extending from the pulp cavity to the apical foramen at the apex or tip of the root. Look for evidences of blood vessels passing through the root canal to the pulp cavity and to the periodontal membrane. Can you distinguish the fibrous bundles (dental ligaments) which extend across the periodontal membrane from the cementum to the bone of the alveolar wall. Beneath the alveolus observe the mandibular (dental) canal in the bone of the jaw, which contains the dental nerves and vessels.

Draw: showing the relation of the tooth to the structure of the jaw.

DEVELOPMENT OF THE TOOTH. THE LABIODENTAL LEDGE. Examine a frontal section through the head of a 12–14 mm. pig embryo *with a hand magnifier. Observe: the median nasal septum* which divides the nasal cavity into two lateral chambers, the nasal fossae; the tongue, projecting upward into the oronasal cavity from the mid-portion of the mandible; the lateral palatine processes, extending downward on either side of the tongue.

Examine the section with the low power, observing the thickening of the epithelium over the region of the jaw on either side of the tongue. Note the superficial cells of the ridge (dental ledge) and the more deeply stained cells of the basal layer, the stratum germinativum. Examine the two points where the cells of the stratum germinativum are growing downward into the subepithelial tissue. The medial downgrowth is the dental lamina, the lateral downgrowth is the labial lamina. A depression or furrow which appears above the labial lamina, the labiodental furrow, will deepen to form the separation between the lip, or cheek, and the jaw. Identify the large oval sections of the cartilaginous bars, Meckel's cartilages, which support the jaw of the embryo. These cartilages lie close to one another in sections through the anterior portion of the jaw and are more widely separated in sections through the more posterior portions. Note the plates and bars of bone which form the beginning of the bony structure of the jaw. What is the position of this newly formed bone in relation to *Meckel's cartilages?*

Draw: showing the labiodental ledge, the dental lamina, the labial lamina and their relation to the other structures of the jaw.

The Tooth Germ. Examine a section through the head of a 45 mm. pig embryo, using the low power. Observe: the dental lamina, extending from the thickened oral epithelium into the subepithelial tissue; the enamel organ, formed by the growth and expansion of the cells on the border of the dental lamina; the moundlike aggregation of mesenchymal tissue, the dental papilla, on which the enamel organ rests; the position of the cartilaginous plates—Meckel's cartilages; the plates and trabeculae of developing bone which outline the bony structure of the jaw. Compare the developing bone in the section with that observed in the study of intramembranous bone formation (see p. 535). What is the relation of the bone to Meckel's cartilages? What is the relation to the tooth germ?

Draw: showing the appearance, and relations, of the structures observed in the section.

Examine the tooth germ (enamel organ and dental papilla) with the high power. Observe: the enamel organ, a bell-shaped structure consisting of an outer layer of cuboidal cells, the outer enamel cells, and an inner layer of columnar cells, the inner enamel cells. Between the outer and inner enamel cells are the stellate cells with branched processes, which, together with the fluid occupying the intercellular spaces, constitute the enamel pulp. Examine the dental papilla, formed by a condensation *of the mesenchymal tissue immediately beneath the inner* enamel cells. Identify the dental capsule (tooth sac), an extension of the condensed mesenchymal tissue from the papilla about the enamel organ.

Formation of the Enamel and Dentine. With the low power examine a section through a developing tooth in which the enamel and dentine are present. Observe: The changes that have taken place in the dental papilla, noting that the cells are more distinctly stellate or fusiform and that delicate fibers have appeared in the intercellular spaces. This tissue has, also, been invaded by numerous small blood vessels. As this vascularization of the dental papilla continues the tissue assumes, more and more, the condition which is characteristic of the dental pulp. The cells on the periphery of the dental papilla have been *transformed into columnar, dentine-producing structures, the odontoblasts.* The newly deposited portion of the dentine immediately adjacent to the odontoblasts has a clear, homogeneous appearance (predentine) while the dentine, which is more remote from these cells, shows a strong tendency to absorb the basic stains, an indication that calcification of the older portions of the dentine is taking place. The enamel appearing as a deeply stained (calcified) layer resting on the external surface of the dentine. Note the layer of tall, columnar cells (ameloblasts) applied to the external surface of the enamel. These cells are developed from the inner enamel cells of the enamel organ; at the level of the lower border of the dental papilla they will be seen to be continuous with the thin, flattened outer enamel cells. Observe the enamel pulp in which the cells have come to be more definitely stellate in form, with long, branching processes. With the growth of the enamel and dentine, the ameloblast layer is pushed upward, the space occupied by the enamel pulp being correspondingly narrowed. A downward *growth of both the inner and outer enamel cells over the sides of the* dental papilla is to be observed. Identify the tubelike extension of these epithelial cells (Hertwig's sheath) which forms a mould within which the dentine of the root is deposited. Observe the development of the bony structure of the jaw, noting that the trabeculae have united to form a V-shaped trough (alveolar trough) in which the developing tooth is located. At a later period this trough is divided by transverse partitions of bone, into alveoli, each alveolus containing a single tooth.

Draw: showing the structures observed in the section.

With the high power examine the enamel and dentine which have *developed over the crown of the tooth. Observe: the odontoblasts, which* form a membranelike layer on the inner surface of the dentine. Note the long, protoplasmic processes extending from the odontoblasts into the dentinal tubules (dentinal fibers of Tomes). Although it may not be distinguished in the preparation, each tubule is surrounded by a layer of more resistant dentine, the sheath of Neuman. Follow the dentinal tubules and note the manner in which they end in a network of anastomosing branches. Identify the ameloblasts, tall cylindrical cells which rest on the external surface of the enamel. Note the position of the nuclei of these cells, also the uncalcified layer of pre-enamel between the ameloblasts and the calcified portion of the enamel. Delicate protoplasmic processes, the enamel processes of Tomes, may be observed to extend from the enamel cells into the substance of the pre-enamel. Observe the arrangement of the enamel rods. What is the relation of the ameloblasts to the rods?

Draw: showing in detail the structure of the enamel and dentine.

THE TONGUE

Examine a section through the body of the tongue with a hand magnifier. Note: the general outline of the organ, distinguishing between the dorsum and lateral sides; the irregular outline of the surface of the dorsum, due to the presence of the lingual papillae; the bundles of striated muscle which occupy the greater part of the body; the layer of connective tissue underlying the epithelium; the lingual septum, the partition of connective tissue which divides the tongue into lateral halves.

Having observed the form and general arrangement of the tissues, examine the section with the low power. Observe: the type of epithelium that covers the surface of the tongue; the subepithelial layer of fibroelastic tissue, noting that its deep portion is condensed to form the lingual fascia; elevations of the subepithelial tissue, noting the manner in which the epithelium is moulded on these elevations to form the lingual papillae; the bundles of striated muscle. Note the different planes in which these bundles lie. As far as possible identify the muscles to which the fiber bundles belong. Do any of these fibers appear to be branched? Observe the manner in which the muscle fibers end in the lingual fascia.

On the dorsum observe the epithelium with the high power. Identify the filiform and fungiform papillae.

A portion of the submaxillary gland with its duct (Wharton's) may be seen in sections of the tongue immediately anterior to the row of circumvallate papillae.

Draw: showing the entire section in outline, filling in one-half of the drawing with the structural details observed.

Examine filiform and fungiform papillae with the high power, and draw.

Examine a section through a circumvallate papilla with the high power. Observe: the form of the papilla; the deep cleft on both sides of the papilla, representing the furrow by which it is surrounded; the primary papilla, also the secondary papillae which rise from the surface of the primary papilla and penetrate the deep surface of the epithelium. What type of epithelium covers the surface and sides of the papilla, and the sides of the furrow? Note the thinning of the epithelium as it extends into the furrow. Identify the serous glands of von Ebner located in the connective tissue beneath the papilla. Note that some of these glands lie in the connective tissue between the muscle bundles. Trace the ducts of the glands to the floor of the furrow. Locate the taste buds in the epithelium on the sides of the papilla. Are taste buds to be found in the epithelium on the wall of the furrow? Examine the taste buds with the higher powers, identifying the sustentacular cells; the gustatory cells; the gustatory hairs; the gustatory pore.

Draw: showing the structure of a circumvallate papilla, the appearance and as far as it can be observed, the structure of a taste bud.

Examine a section of an injected tongue. Observe: the large branches of a lingual artery which are to be seen in the connective tissue attached to the base and sides of the tongue; the capillary distribution to the muscles and glands; the vessels which belong to the vascular plexus in the submucosa; the capillary loops in the primary and secondary papillae.

Construct a diagram, based on the above study, of the distribution of blood vessels in the tongue.

The Soft Palate

Except for its relation to the bone by which it is supported, the mucous membrane of the hard palate is structurally similar to the mucous membrane of the lip and cheek. For the study of the structure of the soft palate, use longitudinal sections of the uvula.

Examine such a section with the low power, observing the epithelium. *Is the epithelium the same on the oral and pharyngeal surfaces?* On which of these surfaces does the epithelium appear to be thicker? At what point is the epithelium most deeply papillated? Note the change in the character of the epithelium on the upper part of the pharyngeal surface. Note the delicate character of the tissue immediately beneath the epithelium. Why is this tissue called a tunica propria? Observe the coarser fibers of the submucosa. Observe the numerous mucus-secreting glands which are present in the submucosa of the oral surface. Are they as abundant in the submucosa of the pharyngeal surface? Identify the bundles of transversely cut striated muscle fibers which form a muscular partition between the oral and pharyngeal sides of the uvula. These fibers belong to the *azygos uvulae muscle. Striated* fibers may be seen extending into the upper part of the section. These belong to the tensor palati and levator palati muscles. Note that the glandular and muscular tissues are not present in the tip of the uvula, which is occupied by loosely arranged fibrous tissue containing a number of thin-walled blood spaces and small masses of fat.

Because of the thinness of their walls, the blood vessels in the tip of the uvula are readily distended. Under certain conditions these vessels are congested, the tip becoming swollen and sensitive.

The Pharynx

Sections for this study should be made through both the larynx and pharynx at about the level of the vocal cords. In such sections the pharynx will appear as an elongated, slitlike opening behind the larynx, surrounded by fibrous and muscular tissues. Examine the pharyngeal portion of the section with the low power. Observe: the layer of stratified squamous epithelium which forms the lining of the pharynx; the delicate, loosely arranged connective tissue fibers forming the tunica propria on which the epithelium rests; the papillae from this layer which penetrate the deep surface of the epithelium. Do these papillae produce any change in the form of the free surface of the epithelium? Examine the bundles of striated muscle fibers, noting their position on the posterior and lateral walls of the pharynx. Can a division of these fibers into definite layers be observed? What is the direction of the muscle fibers in different parts of the muscular layer? On the anterior wall of the pharynx observe the submucosa which consists of a layer of coarse, fibroelastic tissue, external to the tunica propria. Does the submucosa extend between the tunica propria and the muscular tissue on the posterior and lateral walls? Identify the bundles of striated fibers which may be seen in the section, between the submucosa of the pharynx and the larynx. These fiber bundles belong to the laryngeal muscles. Locate the groups of mucus-secreting glands which are in the submucosa. Examine the layer of loosely interwoven connective tissue fibers external to the muscular layers, containing blood vessels, nerves and small quantities of fat. This tissue gives support to the posterior and lateral walls of the pharynx by attaching them to adjacent structures. Note that the submucosa, on the anterior wall, merges with the connective tissue which binds the pharynx to the larynx.

THE ESOPHAGUS

Examine a cross section of the esophagus with the low power. What type of epithelium lines this structure? Is it a relatively thick or thin layer? Observe its attached surface, is it papillated? Can you find a basement membrane? Identify the tunica propria on which the epithelium rests. How can you identify this as a tunica propria? Observe the amount of lymphoid tissue in this layer. Is it in the form of diffuse aggregations or of nodules? Identify the muscularis mucosae. What type of muscle forms this layer? Are the fibers directed circularly or longitudinally? Observe the submucosa, a layer of loosely interwoven collagenous and elastic fibers which supports blood vessels, lymphatics and small bundles of nerve fibers. Note the manner in which the submucosa forms a series of folds that give the lumen its irregular outline. Note how the tissues of the mucosa are carried over the folds. Identify groups of mucous-secreting glands in the submucosa. Wherever possible trace the ducts of these glands to the surface of the epithelium. Note the ampullalike enlargements of the ducts just below the muscularis mucosae. Examine the muscular coat (muscularis externa), noting that it consists of an inner layer of circularly disposed muscle fibers and an outer layer of longitudinal fibers. Which of the two layers is the more strongly developed? What type of muscle forms the muscularis externa in this section? How does the type of muscle change throughout the length of the esophagus? Observe the manner in which the muscle fibers are collected into bundles, which are partially separated by septa of connective tissue. Note the connective tissue septum between the two layers. Examine the adventitia, an external layer of loose areolar tissue containing blood vessels, nerves and small masses of fat cells. Identify groups of ganglion cells: those located in the septum between the circular and longitudinal layers of the muscular coat (myenteric; Auerbach's plexus), and those located in the submucosa (submucous; Meissner's plexus). The cells of the submucosa plexus are often difficult to discover in sections. Note, also, the small bundles of nerve fibers in the septa between the muscle bundles and in the submucosa.

Draw: showing the structure of the esophagus as seen in the section.

Examine sections from the upper, middle and lower thirds of the esophagus. Compare these sections and note the differences in structure. Draw.

THE GASTROESOPHAGEAL JUNCTION

Examine a longitudinal section through the esophagus at its junction with the stomach, using the low power. Observe: the abrupt change from a stratified squamous to a simple columnar epithelium, indicating the point where the esophagus ends and the stomach begins; the continuation of the submucous and muscular coats of the esophagus into the wall of the stomach without any marked change. The mucosa increases in thickness and the muscularis mucosae becomes somewhat disorganized in making the transition. In some sections branched cardiac glands may be seen in the tunica propria of the esophagus, beneath the much thinned out stratified squamous epithelium. The glands which lie beneath the simple columnar epithelium of the portion of the section which belongs to the wall of the stomach are similar to the cardiac glands of the esophagus. Note the increased thickness of the circular muscle layer, which forms a sphincter at the point where the esophagus joins the stomach.

Draw: showing the change which takes place at the gastroesophageal junction as seen in the section.

THE STOMACH

Using the low power, examine sections of both fundus and pylorus. Observe the gastric pits which are diagnostic of stomach. Attention should be called to the relatively straight surface line of the lumen (the pits, which are invaginations, start at the surface level). Identify those layers which are common to the entire alimentary tract: the mucosa, muscularis mucosae, submucosa, muscularis externa, and either a serosa or an adventitia. Compare the thickness of these layers in the stomach with those of the esophagus. After observing these general structural characteristics of stomach, the fundic and pyloric regions should be studied separately.

THE FUNDUS. Examine sections from the wall of the fundus of the stomach with the low power. Observe the mucosa. What type of epithelium is found lining the fundic region? Note the tunica propria which is a thick layer of reticular tissue containing a large number of lymphocytes. Notice the gastric pits which are short and wide in the fundic region. Verify this description and compare them with the gastric pits of the pyloric region. Examine the gastric glands. What type of glands are they and how can you be sure of this classification if the section is an oblique cut? Do these glands extend beyond the tunica propria? Where do they empty? Note the narrow portion by which they are connected with the pits, the neck; the longer and more expanded portion which forms the body; the still more enlarged, blind end of the gland or fundus. Find glands which show a bifid condition of the deep portion of the gland. Note how the amount of reticular tissue in the tunica propria is reduced by the close-set arrangement of the glands. Identify the muscularis mucosae. Note the type of muscle and its arrangement. Is it a relatively thick layer? Observe the submucosa which consists of a loose arrangement of fibroelastic tissue, which gives support to blood vessels, small bundles of nerve fibers and lymphatics. Owing to the thinness of their walls, the lymphatics cannot be distinguished from the surrounding connective tissue. Examine the muscularis externa. Identify an outer layer of longitudinal fibers and an inner layer of circular fibers; also bundles of obliquely directed fibers which lie internal to the circular layer. Observe the serosa which consists of a thin layer of serous cells supported by a substratum of connective tissue. Note the presence of blood vessels and small bundles of nerve fibers in the connective tissue of the serous coat.

Draw: showing the structure of the wall of the fundus as seen in the sections.

Using the same section, examine the mucous membrane with the high power. Follow the epithelium from the surface into the pits. Is there any apparent change in height or appearance of the cells? Follow this epithelium into the gastric glands. How does it compare in appearance with the epithelium of the pits? Observe the types of cells in the glandular epithelium; the neck cells, noting their low columnar form, their relatively clear protoplasm and the flattened nuclei located in their basal ends; the chief cells, which are columnar cells bordering the lumen of the gland. Note their pyramidal form where they can be seen in cross sections of the gland; the fine, deeply staining granules with which their cytoplasm is filled; the round, basally located nuclei. What is the staining reaction of these cells? Owing to the solvent action of some of the reagents employed in preparing the tissue, it frequently happens that the zymogen granules have disappeared from the cell. Identify the parietal (acidophilic) cells which are more or less spherical or triangular in form, and lie between and somewhat peripheral to the chief cells. Note their red color due to their marked affinity for the acid stains; the coarse, highly refractive granules with which their cytoplasm is filled. In what part of the gland are the parietal cells most abundant? Identify the smooth muscle fibers located in the tunica propria between the glands. Observe the small aggregations of lymphocytes in the tunica propria close to the muscularis mucosae. Are they ever arranged in the form of nodules?

Draw: showing the histological structure of the gastric glands.

THE PYLORUS. Examine a section through the pylorus of the stomach with the low power. Observe the mucosa, noting that the epithelium by which it is covered is similar to that in other parts of the stomach. Identify the tunica propria. What is the distribution of the lymphocytes in this layer? Observe the gastric pits. How do they differ in shape from the pits of the fundic region? What type of glands is found in the pyloric region? What is their relation to the gastric pits? Identify the muscularis mucosae, submucosa and muscular externa. How many layers of muscle can you distinguish in the muscularis externa? Note the arrangement of the fibers in each layer. Compare the thickness of each layer with the corresponding layer in the fundic area. Are bundles of obliquely directed fibers present in the pyloric region? What layer or layers contribute to the formation of the pyloric sphincter? Identify the serous coat which forms the external investment of the gastric wall.

Draw: showing the structural appearance of the pyloris as seen in the section.

Examine the pyloric mucosa with the high power. Observe the epithelium lining the gastric pits. Note the depth to which the pits extend in the mucosa. Observe the pyloric glands, two or three of which open into a single pit. Note that each gland consists of a single, short tube or neck which divides into a number of branches. The branches continue (or subdivide) to form the secreting tubules which, owing to their length, are coiled about on the inner side of the muscularis mucosae. These tubules are cut transversely or obliquely in the section. Note the nongranular character of the cytoplasm of the cells lining the tubules; the flattened nuclei, which are located in the basal portions of the cells; the large lumen of each tubule. What kind of a secretion do these glands produce? Are parietal cells to be observed in the pyloric glands? How does the amount of reticular tissue in the pylorus compare with that in the fundus?

Draw, showing the histological structure and relations of the pyloric glands.

THE BLOOD SUPPLY OF THE GASTRIC WALL. With the low power, examine a section from the wall of a stomach in which the vessels have been injected. Observe: the blood vessels located in the connective tissue of the serosa; the branches of these vessels in the connective tissue septa between the muscle bundles of the muscularis externa, noting the distribution of the capillaries to the muscle fibers; blood vessels, some of which are quite large, in the submucosa. Wherever possible trace branches of these vessels through the muscularis mucosae into the mucosa. Note the arrangement of the capillaries about the glands.

Make a diagram, based on the above observations, showing the distribution of blood vessels in the wall of the stomach.

THE NERVES IN THE GASTRIC WALL. Examine sections of both the fundus and pylorus with the high power. Note the small bundles of nerve fibers in the serosa; in the septa between the muscle bundles; in the septum between the inner circular and outer longitudinal layers; in the submucosa. Identify the groups of ganglion cells in the intermuscular septum, the myenteric (Auerbach's) plexus. Similar groups of ganglion cells belonging to the submucous (Meissner's) plexus should be sought in the submucosa. These cells are fewer in number and more difficult to find.

Draw: showing the arrangement of the nervous elements in the wall of the stomach.

THE GASTRODUODENAL JUNCTION

With the low power examine a longitudinal section through the junction of the pylorus with the duodenum. Observe: that the mucosa of the pylorus is relatively deep and contains branched tubular glands which lie internal to the muscularis mucosae, while that of the duodenum is somewhat thinner and contains simple tubular glands (crypts of Lieberkühn). Note that at the point of transition, the tubules of the pyloric glands break through the muscularis mucosae and begin to lie in the submucosa. Glands similar to those observed in the pylorus, but with a more complicated system of branching, are located in the submucosa of the duodenum (Brunner's glands). Note that the inner circular muscle layer has increased in thickness at the point where the transition takes place, the pyloric sphincter.

Draw: showing the changes that take place in the transition from the pylorus to the duodenum.

The Small Intestine

Using the low power, examine sections of duodenum, jejunum and ileum. Identify and observe the villi which are diagnostic of the small intestine. Note that the base line of the villi is relatively straight (these structures are evaginations of the mucosal tissue) while the tips of the villi extend for variable distances into the lumen. Note the variation in the diameter of the intervillus space. Compare the height and shape of the villi in the three areas of the small intestine.

Using high power observe both longitudinal and cross sections of villi from different areas of the small intestine. Observe the epithelium which extends over the villus, noting that it is a continuation of that which lines the intestinal canal. Do you find any goblet cells intermingled with the other cells of the epithelium? Follow the epithelium of the villus into the crypts of Lieberkühn. Do goblet cells occur in these crypts as well as in the epithelium over the villi? Note the tunica propria by which the epithelium of the villus is supported. Observe the presence and distribution of lymphocytes in this tissue. In sections prepared with special stains, plasma and mast cells, as well as a few granulocytes, may also be seen in this tissue. Identify the lacteals, which are lymphatic vessels which start as blind-end capillaries in the villi. They appear in the reticulum as clear spaces lined by thin endothelial cells. Note the smooth muscle fibers lying parallel with the long axis of the lacteals. What is the function of these fibers?

Draw, showing the histological structure of a villus as seen in both longitudinal and cross sections.

THE DUODENUM

Examine a section of the duodenum with the low power. Observe the epithelium, which consists of tall columnar cells. Note the shape and position of their nuclei. Notice, also, the thickness of the tunica propria. Is it a relatively thick or thin layer? Compare it with this layer in other portions of the alimentary tract. In the section of the duodenum note the numerous lymphocytes scattered throughout the tissue. Note that the villi are epithelial covered projections of reticular tissue. The reticular tissue forms a supporting core for the epithelium. Observe the crypts of Lieberkühn which are simple tubular glands that open to the surface of the epithelium between the villi. Note that the cells which line the crypts are continuous with the epithelium of the surface of the mucosa. Identify the muscularis mucosae. In the region of Brunner's glands notice the disturbance in the arrangement of this layer which is produced by the glands and their ducts. Note, also, that a considerable amount of reticular tissue lies between the blind ends of the crypts and this layer. Small aggregations of lymphoid tissue and a few solitary nodules are to be found in the reticular tissue in the region of the muscularis mucosae. Identify the submucosa, the connective tissue of which is largely obscured by the presence of the numerous, coiled branches of Brunner's glands. Note that the ducts of these glands have a relatively wide lumen. Trace the ducts to their connections with the ends of the crypts of Lieberkühn. A few of the ducts may be found to open into the sides of the crypts. Observe the muscularis externa which consists, as in the other parts of the alimentary canal, of an inner circular and an outer longitudinal layer of smooth muscle fibers. Identify and follow the serous membrane, which may be attached to one surface of the duodenum; the outer covering of the remaining surfaces being an adventitia of loosely interwoven connective tissue.

Draw: showing the general stuctural characteristics of the duodenum as seen in the section.

Examine the following structures with the high power: the cells which form the epithelial lining of the duodenum, noting the goblet cells which are interposed between the epithelial cells; the changes which take place in the epithelial cells as they pass from the surface into the crypts of Lieberkühn. Observe the cells of Paneth, which can be identified in the fundi of the glands by their coarse granules stained a deep red by the acid dye. Where in the epithelium are these cells located? Note the form and appearance of the cells which line a tubule of Brunner's glands as seen in cross section. Locate groups of ganglion cells belonging to the myenteric plexus, which are to be found in the connective tissue between the two layers of the muscular coat. Identify similar groups of ganglion cells in the submucosa belonging to the submucous plexus. Why are these cells somewhat difficult to find?

Draw: showing the histological character of the above-mentioned structures.

In a longitudinal section of the duodenum identify the plicae circulares. What layers contribute to the formation of these folds? Note the relation of the villi to the plicae. How do these folds vary in height throughout the extent of the duodenum? Compare the plicae in the jejunum and the ileum.

THE JEJUNUM

With the low power examine a longitudinal section through the mid-portion of the jejunum. Observe: that the arrangement of the mucosa, submucosa, muscularis externa and serosa are the same as described in the general plan of structure of the alimentary canal. Identify the tall, narrow folds, the plicae circulares, which are formed by elevations of the submucosa. Note the manner in which the structures of the mucosa are carried over these folds. Where the section passes through secondary and tertiary folds, the plicae appear to be branched. In the mucosa observe the presence of masses of diffuse lymphoid tissue and solitary nodules. Examine the serosa which consists of a layer of thin, flattened mesothelial cells supported by a substratum of connective tissue.

How does the mucosa compare in thickness with that of the duodenum? Does this affect the length of the crypts of Lieberkühn? Compare the form of the villi in the jejunum with those found in the duodenum. How does the wall of the jejunum compare in thickness with that of the duodenum?

Draw: showing the characteristic structure of the jejunum as seen in the section.

THE ILEUM

With the low power examine a longitudinal section of the ileum through a Peyer's patch. Observe a portion of the wall of the ileum which is devoid of masses of lymphoid tissue, comparing the arrangement of the coats, the villi and the crypts of Lieberkühn with those observed in the duodenum and jejunum. Locate and examine a Peyer's patch, which consists of large aggregations of lymph nodules. Note the form of the nodules; their position in both the mucosa and submucosa; their germinal centers; the diffuse lymphoid tissue with which the spaces between the nodules are filled. How much of the nodule lies in the submucosa? Can any portion of the muscularis mucosae be seen between the nodules? What is the condition of the epithelium above the mass of lymphoid tissue? Can lymphocytes be seen which are migrating between the cells toward the surface of the epithelium?

Draw. (a) showing the structure of the wall of the ileum outside the area of lymphoid aggregations; (b) the wall of the ileum where the section passes through a Peyer's patch.

THE ILEOCOLIC (ILEOCECAL) VALVE

The walls of both the small and large intestines join to form two lips, one above the other, bounding the slitlike aperture through which the contents of the ileum pass into the large intestine (colon). These lips form a valvelike structure (*ileocolic valve*), the closure of which prevents the food, once it has been received by the colon, from passing back into the ileum.

With the low power examine a section which passes lengthwise through the ileocolic valve. Observe the mucosa as it appears on both sides of the valve. The mucosa on the sides of the lips of the valve which are opposed to each other, belongs to and is characteristic of the ileum. Note that it forms a relatively thick layer and presents crypts of Lieberkühn, low conical villi, aggregations of lymph nodules and a muscularis mucosae. The mucosa on the opposite sides of the lips presents no villi but is supplied with wide crypts, the epithelium of which contains numerous goblet cells. Follow the muscularis mucosae as it passes from the ileum over the border of the lip and becomes continuous with the muscularis mucosae of the colon. In the same manner the submucosa of the ileum becomes continuous with the submucosa of the colon. The inner circular layer of smooth muscle fibers extends into the lips of the valve where it forms a small sphincter muscle which aids in the closure of the valve. The outer longitudinal layer of muscle fibers also extends into the lips of the valve, in which it meets and joins the corresponding layer from the colon.

Draw: showing the structure of the ileocolic valve.

THE LARGE INTESTINE

Using the low power, examine sections from various areas of the large intestine. Note that these sections have neither gastric pits nor villi. The large intestine is characterized by the presence of crypts of Lieberkühn.

THE COLON

Examine a cross section of the colon with the low power. Observe the epithelium, consisting of tall columnar cells forming the surface tissue of the mucous coat, and the reticular tissue (tunica propria) on which the epithelium rests. Identify the crypts, which are simple tubular glands formed by the invagination of the epithelium. Note the number of goblet cells in the epithelium lining the crypts. Observe the strongly developed muscularis mucosa, noting the number of layers of smooth muscle of which it consists. Examine the relatively thick submucosa. Note the folds formed by the submucous and mucous coats that give an irregular outline to the lumen. What is the direction of these folds? Are they temporary or permanent? Observe the circularly arranged inner layer of smooth muscle fibers of the muscular coat. How does it compare in thickness with the corresponding layer in the small intestine? Identify the taeniae coli. What are they and how are they formed? Note the manner in which the longitudinal muscle layer becomes thinner on either side of the taeniae. Identify the adventitia, consisting of loosely arranged connective tissue fibers. Note the blood vessels and small bundles of nerve fibers in this layer. In some sections of the ascending and descending divisions of the colon a serous membrane may be present on its outer surface. Because of its more or less complete investment by the mesenteric extension of the peritoneum, the transverse colon always presents a serous membrane as its outer covering. Locate and examine the epiploic appendix, noting the narrow stalk or peduncle by which it is attached to the wall of the colon; the flattened mesothelial cells by which the connective tissue and fat cells contained in the epiploic appendix, are enclosed; the blood vessels in the connective tissue between the lobules of fat; the large lymph node in the expanded portion of the appendix. In many cases a lymph node may not be present.

Draw: showing the structure of the wall of the colon; a few of the crypts as seen with the high power; an epiploic appendage.

THE VERMIFORM APPENDIX

Examine a section of the vermiform appendix with the low power. Observe the lumen, noting its irregular outline due to the folding of the submucous coat. Identify the crypts; note that they are similar to those in the mucous membrane of the colon, except that they do not contain as many goblet cells and that they are frequently divided into two or three simple branches. Is there much lymphoid tissue in the tunica propria? Note the number of nodules present; their germinal centers; the diffuse lymphoid tissue by which the nodules are surrounded. How much of the muscularis mucosae can be observed? Identify the submucosa, the greater part of which is obscured by the lymphoid tissue which extends into it from the mucous membrane. Observe the muscular coat; does it present the same arrangement of smooth muscle fibers as in the small intestine and colon? Examine the serous coat, a layer of mesothelial cells, supported by a substratum of connective tissue which is continued about the wall of the appendix from the mesoappendix. Identify the vessels and nerves in the mesoappendix by which the wall of the vermiform appendix is supplied.

Draw: showing the appearance and structure of the vermiform appendix as seen in the section.

THE RECTUM

Examine a cross section of the rectum with the low power. Note that its structure resembles that of the colon. However, the following differences should be observed: the crypts of the rectal mucosa are longer and wider than those in the mucosa of the colon; goblet cells are present in such numbers that they constitute the greater portion of the epithelial elements of the crypts; the fibers of the longitudinal muscle are present in the form of a continuous layer about the wall of the rectum. Note the manner in which the longitudinal muscle layer is thickened on the anterior or posterior wall of the rectum, or both.

Draw: showing the structure of the rectal wall as seen in the section.

Examine a longitudinal section of the rectum with the low power. Observe the rectal folds (valves of Houston). The valves are three in number, one being located on the right and two on the left side of the rectal wall. Note that not only the mucosa and submucosa, but both the muscular layers are included in the structure of these folds; a portion of the longitudinal muscle extending downward across the base of the fold for the purpose of giving it added support.

Draw: showing the structure of the valves of Houston.

THE ANAL CANAL

Examine a longitudinal section through the anal canal with the low power. Observe: the changes in the epithelium lining the different regions of the canal; the simple columnar epithelium in the rectal portion. Note that it rests on a tunica propria, which is separated from the submucosa by a muscularis mucosae. The mucous membrane also contains a number of crypts of Lieberkühn. Note the stratified columnar epithelium which covers the upper part of the columnar area. This epithelium is best seen in places where the section passes through the anal sulci or grooves between the columns. Observe the stratified squamous epithelium which lines the intermediate area of the anal canal; the thin epidermal layer which covers the cutaneous surface. Occasionally the anal sinuses or blind pouches formed behind the anal valves by the lower ends of the sulci, can be seen in the section. What kind of epithelium forms the lining of the anal sinuses? Observe the firmly compacted connective tissue on which the epithelium of the intermediate and cutaneous areas rests.

Observe the disposition of the muscular tissues in the wall of the anal canal. Identify the dilator muscle of Rudinger. Note the manner in which fiber bundles from the muscularis mucosae of the rectum are continued into the anal columns to form this muscle. Observe the thickened muscular ring formed at the lower end of the circular layer of smooth muscle, the internal sphincter muscle of the anus. Note the position of this muscle in relation to the anal valves. Identify the external sphincter muscle which appears as transverse sections of striated fibers below and external to the internal sphincter. Trace the course of the fibers of the longitudinal smooth muscle layer between the sphincter muscles, noting that the delicate, tendinous fibers, in which this muscle is continued, end in the corium. Identify the obliquely directed striated fibers of the levator ani muscle in the external border of the section. Note the tendinous fibers by which this muscle is attached to the fibrous tissue of the canal.

OBSERVE THE GLANDS OF THE ANAL CANAL. Identify fragments of the intramuscular glands in the connective tissue septa between the bundles of the circular muscle layer. If present, the duct will be directed toward the epithelium which lines the intermediate area. Note the type of cells and the number of cell layers in both the secreting tubules and the duct. Identify sebaceous glands close to the border of the anal opening. Identify the anal glands of Gay, which are large coiled tubular glands in the region external to the border of the opening. Note the hair follicles, sebaceous glands and sweat glands in the tissue beneath the epidermis of the cutaneous area, as well as the lymph nodules and blood vessels (branches of the hemorrhoidal arteries and veins) in the submucous tissue underlying the rectal mucosa.

Draw: showing the histological structure of the anal canal.

METHOD OF IDENTIFICATION OF SEGMENTS OF THE ALIMENTARY TRACT

The identification of the various segments of the alimentary tract seems to cause most students considerable difficulty. With reasonably careful observation of certain structural characteristics this can be avoided.

First, it is essential that students learn to differentiate between villi and gastric pits. *This in itself is not difficult if the student remembers that gastric pits are invaginations from the surface level while the villi are evaginations beyond the surface level. Compare villi and gastric pits in sections.*

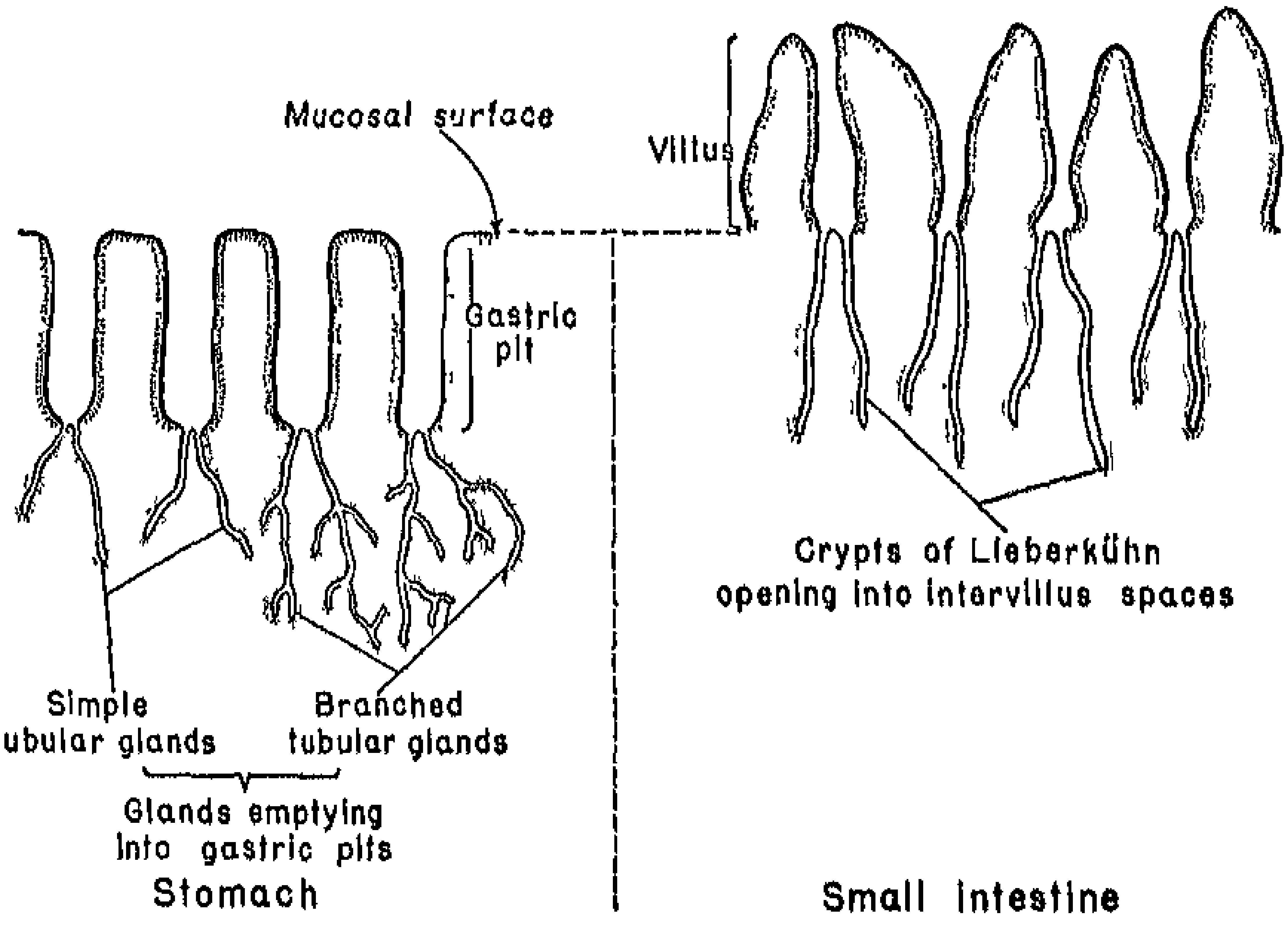


FIG. 297

Given an unknown section, one surface of which is covered by an epithelium.

Check to see if there is a muscularis mucosa. If there is it *must* be a section from the alimentary tract.

Identify the type of epithelium. If it is stratified squamous it must be esophagus or anus. If it is a simple columnar epithelium it must be the tract between the gastroesophageal junction and the rectoanal junction.

With a stratified squamous epithelium it is now necessary to differentiate between esophagus and anus. Examine the remaining layers. If they are uniform and conform to the general orderly arrangement of the digestive tract, particularly the muscularis externis, it is undoubtedly esophagus. Observe the type of muscle in the muscularis externis in order to determine the level at which the section was taken. If both layers are striated muscle it is from the upper one-third, if there is both smooth and striated muscle present, it is from the middle third, and if it is almost entirely smooth muscle it is from the lower one-third.

Irregular arrangement of layers, presence of some stratified columnar epithelium, hair follicles and sebaceous glands would be diagnostic of anus.

If, on the other hand, the epithelium is a simple columnar epithelium the student should check for the presence of the following: (a) gastric pits, (b) villi or (c) simple tubular glands (crypts of Lieberkühn) only. By doing this it is possible to quickly assign the section to the region to which it belongs.

If gastric pits are present it must be stomach. Next identify the type of glands. If they are simple tubular it is a section from the fundus. (Note the presence of parietal cells, which should be there in quantity.) Branched tubular glands would identify the section as pylorus.

The presence of villi could *only* mean small intestine. It only remains to decide if it is duodenum, jejunum, or ileum.

Look for Brunner's glands in the submucosa. If they are present it *must* be duodenum. However, some sections of duodenum have *no* Brunner's glands. Therefore, it is necessary to check the shape of the villi. In the duodenum they are tall and leaf-shaped. The mucosal layer *is also thickest in the duodenum. Ampulla of Vater, if it is present, is* also a positive diagnostic characteristic for duodenum.

Check for the presence of Peyer's patches. If they are present it must be ileum. However, here again, it may be ileum without Peyer's patches. Observe the villi. In the ileum they are shortest and are club-shaped. The plicae circulares are also short and relatively broad.

If you have systematically ruled out duodenum and ileum, then observe the plicae circulares. Tall, thin, branching plicae are diagnostic of jejunum. The villi are moderately tall and conical.

If there are neither gastric pits nor villi, but only simple tubular glands present in the mucosa it must be large intestine. If it is a cross section look for the thickenings in the longitudinal layer of the muscularis externis. If there are three such thickenings it must be colon. If there is only one or two strongly developed longitudinal thickenings it must be rectum. Examine the glands. They are somewhat shorter and narrower in the colon and there are fewer goblet cells. This last criterion, however, must be a relative evaluation unless it is known that both sections were taken from the same person or animal and, therefore, it may be difficult for the beginning student to evaluate properly.

STUDY OF GLANDS ASSOCIATED WITH THE DIGESTIVE TRACT

The Salivary Glands

THE PAROTID GLAND

Examine a section of the parotid gland with the low power. Observe *the connective tissue septa by which the gland is divided into lobes and* lobules. Note that the septa are extensions of the capsular tissue which envelops the gland. Identify blood vessels and nerves located in the capsule and in the septa. Study the duct system and from your observations construct a diagrammatic representation of this system. Observe the interlobar ducts located in the broader septa between the lobes. What type of epithelium lines these ducts? Follow the septa as it extends between the secondary and primary lobules. Identify the interlobular ducts. What type of epithelium lines these ducts? Observe the intralobular ducts located within the lobules. Note the epithelium which forms their lining. Note that the intralobular ducts are surrounded by a small amount of connective tissue. Identify the intermediate (intercalary) ducts. Note their narrow lumen and the type of cell which forms their epithelial lining. Observe the acini which consists of pyramidal cells arranged about a small opening or lumen.

Examine several acini with the high power. Observe the form and arrangement of the cells; the finely granular character of their cytoplasm; the form, position and staining quality of their nuclei. What kind of a secretion do these cells produce? What effect does the secretory activity of these cells have on the quantity of these granules? By observing the cells carefully can you recognize acini in the resting stage and those in the secretory stage?

Observe the cells which form the epithelium of the intermediate ducts. Note that the flattened epithelial cells of the intermediate ducts are continuous with the pyramidal cells of the acini.

Can basket cells be identified (by the position, shape and staining properties of their nuclei) in the walls of the smaller ducts? Is there any difference in the appearance of the cells of an acinus arranged about a lumen that is scarcely perceptible, and those arranged about a larger, *more distinctly visible lumen? What is the staining* reaction of these cells?

Draw: showing the structural characteristics of the acini and their associated ducts as seen with the high power.

THE SUBMAXILLARY GLAND

Examine a section of a submaxillary gland with the low power, following the outline for the low-power study of the parotid gland. Note that in addition to the serous acini there are groups of mucous acini scattered throughout the substance of the gland. How are the mucous acini to be recognized?

Examine the section with the high power. Observe: The serous acini; note their similarity to those observed in the parotid gland; the mucous acini; note their arrangement in small groups; the pyramidal form of their cells; the flattened nuclei which, together with a small amount of cytoplasm, have been pressed by the accumulated mucoid material into the basal portion of the cell. Identify the crescent-shaped demilunes; note their relation to the cells of the mucous acini; their deeply staining, spherical nuclei; the fine, basophilic granules in the cytoplasm. What kind of a secretion do they produce? Where is their secretion emptied? Name the points by which serous acini can be distinguished from mucous acini.

Draw a group of serous and mucous acini which are adjacent to one another, showing their structural characteristics. Include mucous acini which show demilunes.

THE SUBLINGUAL GLANDS

Examine a section of a sublingual gland with the low power, following the directions given for the study of a salivary gland. Make the following observations: that the mucous acini greatly predominate over the serous acini; that demilunes are abundantly present in association with the mucous acini. Compare the duct systems of these three salivary glands. How do they differ?

Draw: showing the structural appearance of the mucous acini and their associated demilunes as seen with the high power.

THE BLOOD SUPPLY OF A SALIVARY GLAND

Examine a section of an injected gland with the low power. Make the following observations: the position of the blood vessels in the capsule and septa, the capillaries, noting their position in relation to the acini and ducts, and that those about the acini are closely applied to the basement membranes.

On the basis of the above observations construct a diagram showing the distribution of the blood vessels in a salivary gland.

THE PANCREAS

1. Examine a section of the pancreas with the low power. Observe: the division of the gland into lobules; distinguishing between the

primary and secondary lobules as far as possible. Note that the primary lobules are not completely separated by the septa of connective tissue which extend between them. Identify the principal duct of the pancreas (duct of Wirsung) which may be observed in sections which have been cut in the proper plane. What type of epithelium lines this duct? Note: that its epithelium rests on a delicate basement membrane; that the remainder of the wall consists of densely compacted fibrous tissue. Identify smooth muscle fibers in the wall of the duct. Observe the interlobular ducts, which are branches of the pancreatic duct which may be followed into the septa between the secondary and primary lobules. The larger ducts are lined by what type of epithelium? The epithelium of the smaller ducts consists of what types of cells? Observe the intermediate (intercalary) ducts, which are branches of the interlobular ducts which are located in the lobules. Note that the intermediate ducts take the place of intralobular ducts in the pancreas. Note, also, that they closely resemble the intermediate ducts of the salivary glands. Identify the islands of Langerhans, noting that the islands are considerably lighter in color than the surrounding tissue of the pancreas.

Draw several lobules, showing the structural appearance of the gland as seen with the low power.

2. *Examine the section with the high power.* Observe: the acini, noting the different planes in which they have been sectioned; the acinar cells, noting their spherical nuclei; the location of the nuclei in the cells; the coarse, acidophilic granules in the portion of the cell which is toward the lumen of the acinus; the darker, basal zone from which granules are usually absent. Identify the centroacinar cells. Where are they located? Note their size, shape and staining reaction. What is their relation to the acinar cells? Observe several islands of Langerhans. What is the shape of the cells and how are they arranged? How many distinct types of cells are present in the islands? Identify cells of each type and note their morphological characteristics. How do these cell types differ in number and location in the islands? What secretion is produced by the endocrine portion of the pancreas? What is its importance in the body? Note the sinusoids which occupy the spaces between the cell cords; also the delicate investment of connective tissue by which the islands are separated from the surrounding tissue of the pancreas. Observe the ducts, which are tubular structures located in the septa between the lobules. Note that the larger ducts are lined by tall columnar cells, and that the cells become lower in the smaller ducts until, in the ducts between the primary lobules, they are cuboidal in form. Note, also, the fibrous tissue which forms the walls of the ducts external to the epithelium. The intermediate ducts can be seen in the lobules. They are to be identified by their narrow lumina

and low, flattened epithelium. Find a place in the section where the duct is joined to an acinus, noting that the cells of its epithelium appear to be continuous with the centroacinar cells.

Draw, showing (1) the structure and arrangement of the cells in an acinus; (2) The histological structure of an island of Langerhans; (3) Two or more examples of the ducts, showing the character of their epithelium and the thickness of their walls; (4) The junction of an intercalary duct and an acinus.

THE LIVER

PIG'S LIVER. A section of pig's liver is first studied for the reason that the lobules are completely outlined and, therefore, are readily identified. This condition does not exist in the human liver, in which the outlines of the lobules are somewhat obscure.

Examine a section of pig's liver with the low power. Observe: the hepatic lobules, noting the manner in which they are completely outlined by septa of connective tissue (capsule of Glisson); the central veins, occupying a central position in the lobules; the hepatic cords, rows of hepatic cells radiating from the central vein to the periphery of the lobule; the hepatic sinusoids, irregular, thin-walled capillary structures occupying the spaces between the cell-cords; the portal canals, expansions of the connective tissue of Glisson's capsule, occupying "corner positions" between the lobules. Note the presence and position, in relation to each other, of the branches of the hepatic artery, the portal vein and the bile duct.

Draw two or three lobules, including the structures indicated above, as seen in the section.

HUMAN LIVER. Examine a section of human liver with the low power, following the directions for the study of the pig's liver. Note that the lobules are not completely invested by connective tissue and that the hepatic cords of adjacent lobules unite with one another. The portal canals, however, occupy the same position in relation to the lobules, as in the section previously studied. To outline an hepatic lobule in human liver, imagine a line drawn from one portal canal to another enclosing a central vein and the radiating cords of the lobule.

Draw: showing the structural appearance of human liver as seen in the section.

Examine the section with the high power. Observe: the form of the hepatic cells; their arrangement in the hepatic cords; the finely granular character of their cytoplasm; the presence of large vesicular nuclei, noting their spherical form. Locate several cells which show two nuclei instead of the usual single nuclei. Identify the bile capillaries, appearing as small apertures or clefts between the hepatic cells.

In silver nitrate preparations, the bile capillaries in which the silver salts have been precipitated, appear as dark lines extending through the hepatic cords.

Observe *the sinusoids, thin-walled vessels of unequal diameter* occupying the spaces between the hepatic cords. Note the type or types of cells which form the walls of the sinusoids and their closeness to the hepatic cells. In specially prepared material, a layer of delicate reticular fibers can be identified between the endothelial cells of the sinusoids and the cells in the hepatic cords. Frequently, owing to their extreme thinness, the cells lining the sinusoids can be identified only by their bulging nuclei. *Identify the stellate cells of Kupffer,* which may be seen lying across the lumen of a sinusoid. They can be recognized by their large nuclei and stellate form. Locate several portal canals. What forms a portal canal? Note their position in relation to the lobules. Note also the position of the branches of the artery, vein and duct in the portal canal.

Draw: showing the histological appearance of the structures indicated.

Review the circulation of the liver. Examine a section of an injected liver with the low power. Identify the vessels which are present in the section. Diagrammatically reconstruct the vascular supply of the liver.

THE GALL BLADDER

Examine a section of the gall bladder with the low power. Observe: the mucosa; note the tall, columnar cells of the epithelium; the subepithelial layer of delicate, collagenous and elastic fibers. Are reticular fibers present in this layer? If so what is their distribution? Why is this layer called a stroma? How does it differ from a tunica propria. Are goblet cells present in the epithelium of the gall bladder? Do the cells of the epithelium possess true cuticular borders? Note the folds into which the mucosa is raised. Note how the tall, primary folds are joined to one another by secondary folds; also the recesses which are enclosed by these folds. Observe the muscularis; note the manner in which the differently directed bundles of smooth muscle fibers are intermingled in this layer. Identify the *adventitia; note the layer of* densely compacted connective tissue which forms the portion of the wall external to the muscular layer; the loosely interwoven fibrous tissue between the wall of the gall bladder and the surface of the liver. What is the external covering of the portion of the gall bladder that is not opposed to the surface of the liver?

Draw: showing the histological structure of the wall of the gall bladder.

THE BILE DUCT

Examine a section through the bile duct with the low power. Observe: the similarity between the cells which form its epithelial lining and those in the epithelium of the gall bladder. Are true goblet cells present in the epithelium of the bile duct? Examine the stroma, delicate fibroelastic tissue on which the epithelium rests. Observe: a number of small, branched tubular, mucus secreting glands may be found in the stroma; the thin layer of smooth muscle fibers, in which the differently directed bundles do not form definite layers.

Draw: showing the histological structure of the bile duct.

METHOD OF IDENTIFICATION AND DIFFERENTIATION OF LACRIMAL, PAROTID AND PANCREAS

Difficulty is often encountered in distinguishing between lacrimal, parotid and portions of the pancreas in which there are no islands of Langerhans. Given an unknown slide for identification. When examined under low power it is found to be composed of numerous serous acini. It undoubtedly must be lacrimal, parotid or pancreas. The student should first look to see if any islands of Langerhans are present. If he can identify any he can be sure the tissue is from the pancreas. If none are found he must use other criteria for differentiating.

Examine the section to see if there is a definite, well-defined capsule. If one is present it is probably parotid. The septa which extend into the gland should be broad, compact and separate the glands into definite lobes and lobules. The acinar cells should be pyramidal in shape and filled with highly refractive granules.

If there is no well defined capsule it is probably pancreas or lacrimal. Pancreas has only a thin layer of areolar tissue around the gland, from which relatively few thin and incomplete septa extend into the parenchyma. The acini are closely packed and the cells are pyramidal in shape. They differ from cells of the parotid in that they show a more deeply staining basal portion which shows striations, and a more lightly staining area bordering the lumen of the acini. The nuclei are located more basally than those of the parotid gland, and contain one or more well defined nucleoli. Centroacinar cells should be identified and are diagnostic of pancreas.

The connective tissue surrounding the lacrimal gland is not arranged in a compact, definite capsular layer. It is more loosely arranged and the septa are broad and contain numerous lymphocytes. The acinar cells are more columnar than the cells in the parotid and the lumen of the acini are relatively large as compared to the acinar lumen of the parotid. The presence of many basket cells, located between the acinar cells and the basement membrane, is also diagnostic of lacrimal gland. The general effect, under low power, is of definite acinar clusters arranged in small groups and relatively large amounts of loosely arranged connective tissue. Parotid has a much more compact acinar arrangement.

When the routine laboratory study of each of these three glands has been completed, the student should take sections of these three glands and make a comparative study based on the above identification method, until he has firmly fixed in his mind the differentiating characteristics.

STUDY OF THE RESPIRATORY SYSTEM

NASAL FOSSAE

A frontal section through the nasal region of an advanced embryo of a dog, cat or pig will provide satisfactory material for the following study. Similar sections from human embryos should be used whenever they can be obtained.

Holding the section to the light, examine it with a hand magnifier. Observe: the relation of the nasal fossae to the oral and orbital cavities; the median partition (nasal septum) by which the cavity of the nose is divided into right and left chambers (fossae); the conchae, curved processes projecting into the fossae from their lateral walls. Note that both the nasal septum and conchae are supported by plates of embryonic cartilage. Identify the pits or tubular structures seen in the section in the lower part of the nasal septum (Jacobson's organ).

Draw: showing the form of the section and the relation of its parts.

Examine the nasal fossae with the low power. Observe the respiratory portion of the nasal epithelium. Note the two or three rows of oval nuclei belonging to the columnar cells of the pseudostratified epithelium; the round, deeply staining nuclei of the basal cells forming only a single row. Identify the olfactory portion of the epithelium which lines the upper third, or less, of the nasal fossae. Note the single row of oval nuclei (zone of oval nuclei) belonging to the supporting cells, below which are several rows of round nuclei (zone of round nuclei) belonging to the olfactory cells.

In studying the respiratory and olfactory epithelia in this section, it should be remembered that the embryonic character of the tissue makes it more valuable for observing their extent than their histological structure.

JACOBSON'S ORGAN. Note with which type of epithelium, respiratory or olfactory, the lining of the organ more nearly corresponds.

Draw: showing (a) the distribution of the respiratory and olfactory epithelia, as observed in the section· (b) Jacobson's organ (study with the high power).

MUCOUS MEMBRANE OF THE RESPIRATORY REGION. Examine a section through an inferior concha with the high power. Observe: the tall, columnar cells of the epithelium, noting the manner in which their oval nuclei are disposed in two or three rows; a single row of deeply stained, spherical nuclei which indicates the position of the basal cells. Note their location between the basal portions of the columnar cells. Observe the numerous goblet cells interspersed between the cells of the epithelium and the manner in which the epithelium is folded. These folds have been interpreted as being pitlike invaginations which represent vestigial glands. Can any depressed areas lined with mucous cells be seen in the epithelium? Note the clearly defined and apparently homogeneous basement membrane; the subepithelial fibroelastic stroma. Note that this tissue cannot be subdivided into a tunica propria and a submucosa. The tissue which lies directly beneath the epithelium, however, consists of delicate fibers in which numerous lymphocytes are present. The deeper fibers are coarser and merge with the periosteum which covers the bone. Note in the stroma: numerous, large, thin-walled blood vessels which give the stroma the appearance of erectile tissue; mixed serous and mucous glands.

Draw: showing the histological characteristics of the respiratory mucous membrane.

MUCOUS MEMBRANE OF THE OLFACTORY REGION. Examine a section through the upper portion of the nasal fossa, a short distance below the cribriform plate of the ethmoid bone. Use the high power. What type of epithelium lines the olfactory region? Identify the three types of cells present in the olfactory epithelium. In sections where the cell boundaries are not discernible the recognition of the cells can be made from the location and structural characteristics of the nuclei. Observe the sustentacular (supporting) cells. These cells are the most numerous. What is the shape of the nuclei of these cells? In what part of the cell is the nucleus located? Note that they form a single row that is located in the same plane. What is the name of the nuclear zone? Are these cells ciliated? Do they possess cuticular borders? Terminal bars? Can you identify the two areas (superficial and basal) of these cells? How do they differ? What gives the yellowish color to the superficial portion of these cells? Can you identify the forked basal portions of these cells? What is the relation of the basal processes of these cells to the underlying connective tissue? Is there a basement membrane present? Identify the olfactory cells. How would you classify these cells structurally? What is the shape of the nuclei and where are they located in the cells? What is the relation of this zone of nuclei to the zone of nuclei of the sustentacular cells? Observe the olfactory hairs of the cells. What are they, where are they located and what is their function? Compare these cells with bipolar ganglion cells and note what parts are comparable. Identify the small, deeply stained nuclei between the basal portions of the supporting cells. What is the shape of these nuclei? These nuclei indicate the position of the basal cells. What is the character of the cytoplasm of the basal cells? Observe the stroma, similar in general to that of the respiratory region in that it contains blood vessels and lymphatics. Note the branched tubular glands (olfactory glands of Bowman). Two or three of these glands may be found communicating with a large ampullalike structure, the cells of which contain pigment and add to the coloration of the olfactory epithelium. This enlarged structure communicates with the surface of the epithelium by a single duct. Identify the bundles of fibers (filia olfactoria), the extended basal processes (axons) of the olfactory cells—noting their position between the epithelium and the stroma.

Draw showing the histological structure of the olfactory epithelium.

THE LARYNX

THE EPIGLOTTIS. Examine a longitudinal section of the epiglottis with the lower power. Follow the stratified squamous epithelium from the pharyngeal surface over the free border of the epiglottis to the laryngeal surface. Note that below the *aditus* or superior opening of the larynx, the epithelium changes from stratified squamous to the pseudostratified (stratified columnar?) type. Observe the small groups of mixed serous and mucous glands in the connective tissue between the epithelium and the supporting cartilage. Are glands present in the mucous membrane as it passes over the free border of the epiglottis? Note the plate of elastic cartilage which gives support to the mucous membrane of the epiglottis; the considerably thickened connective tissue at the base of the epiglottis, forming the glossopharyngeal ligament.

Draw: showing the structure of the epiglottis.

LARYNX AND PHARYNX

Using a hand magnifier, examine a section through the larynx and pharynx at the level of the vocal cords. Identify: the thyroid cartilage; the cricoid cartilage, noting its position between the wings of the thyroid cartilage; the arytenoid cartilages. What is their position in relation to the cricoid cartilage? The position and structure of the pharynx and its relation to the larynx have already been studied. Observe: the vocal cords, fibrous cords which are attached, anteriorly to the thyroid cartilage, and posteriorly to the vocal processes of the arytenoid cartilages; the thyroarytenoid muscles, striated muscle fibers attached anteriorly to the thyroid cartilage and posteriorly to the sides of the vocal processes of the arytenoid cartilages; the arytenoideus muscles, represented by a mass of striated fibers posterior to the cricoid and arytenoid cartilages.

Study the section with the high power, noting the type of epithelium on the vocal cords.

Draw showing the structure of the larynx as observed in the section.

THE VOCAL CORDS. Hold a longitudinal section of the larynx to the light and examine with a hand magnifier. Observe: the thyroid cartilage, a large plate of hyaline cartilage by which the tissues of the larynx are supported; the large, membranous superior folds (false vocal cords); the inferior folds (true vocal cords). Note that the true vocal cords are somewhat smaller than the false cords; the laryngeal ventricle, the large diverticulum between the superior and inferior folds.

Make an outline drawing of the structures observed. This outline should be sufficiently large to include the details to be observed later.

Examine the section with the low power. Observe: The changes which take place in the form of the epithelium. What kind of epithelium lies upon the superior fold? Over the inferior fold? Below the inferior fold? Observe the subepithelial connective tissue. Note that it consists of delicate fibers both collagenous and elastic, and contains numerous lymphocytes which form diffuse aggregations and nodules. In what portions of the larynx are nodules and diffuse patches of lymphocytes most abundant? Observe the submucosa, consisting of coarser fibers of collagenous and elastic tissue. Note the large, thin-walled blood spaces and small groups of mixed serous and mucous glands. Are glands and lymphoid tissue present in the region of the true vocal cords? Identify the thyroarytenoid ligaments; these ligaments form the true vocal cords. Compare with the transverse section of the larynx previously studied. Note that the cords have been cut transversely, and that the highly refractive ends of the elastic fibers can be seen between the somewhat larger bundles of collagenous fibers. Identify the thyroarytenoid muscle, consisting of striated fibers located between the thyroarytenoid ligament and the thyroid cartilage. Identify the cricoarytenoid muscle, striated fibers appearing between the cricoid and thyroid cartilages. Identify the cricoid cartilage, a narrow plate of hyaline cartilage below the thyroid cartilage. The structure of the mucous membrane below the inferior folds and the form of its epithelium are similar to and are continued in that which occurs in the trachea.

Draw: showing the histological structure of a section through the vocal cords.

THE TRACHEA

Hold a cross section of the trachea to the light and examine with a hand magnifier. Note that it is a membranous tube, the walls of which are supported by incomplete rings of hyaline cartilage. Note that these rings are open toward the esophagus, this portion of the trachea being considerably flattened.

Examine the section with the low power, using the high power when necessary for verifying the more specific details of structure. Observe: the mucous membrane; note that it consists of a pseudostratified (stratified columnar?) epithelium, the free surfaces of the epithelial cells being abundantly suppled wiith cilia. Note, also, that numerous goblet cells are present among the epithelial cells. Identify the tunica propria, a layer of reticular fibers, immediately beneath the epithelium. Note the well-defined basement membrane on which the epithelium rests; the scattered lymphocytes in the tunica propria; collections of lymphoid tissue in the form of diffuse patches and small nodules. In sections which have been prepared with selective stains, numerous elastic fibers will be seen in this layer, and they are especially numerous between the tunica propria and the submucosa. Observe the submucosa, a layer of collagenous and elastic fibers located between the mucous membrane and the tracheal cartilages. Note the blood vessels and nerves contained in this layer; also groups of mucous glands, their serous elements being in the form of demilunes situated externally to the mucous cells. Classify these glands according to structure. Wherever possible, trace the ducts of these glands to their openings on the surface of the epithelium. Observe the posterior part of the wall of the trachea, noting that it consists of a mucous membrane, a submucosa and a layer of circularly directed smooth muscle fibers, the trachealis muscle, which are attached to the free ends of the tracheal cartilages. Note the manner in which the mucous membrane is folded, also the groups of glands in the submucosa. What is the position of these glands in relation to the trachealis muscle? Identify the tracheal cartilage; note that the surrounding connective tissue is condensed on the surfaces of the cartilage to form the perichondrium. Observe the loose adventitial tissue which forms the external investment of the trachea.

Draw: showing (1) the general appearance of the trachea as seen in the section under low power: (2) the details of its structure as seen in the study of a small section of the tracheal wall with the high power.

THE LUNGS

BRONCHI AND BRONCHIOLES

Examine a section through the hilum of the lung with the low power. Branches of the pulmonary and bronchial vessels, lymph nodes, bundles of nerve fibers and a considerable amount of pulmonary tissue may be observed in the section, in addition to the bronchi and bronchioles.

Examine a typical bronchus. Observe the bronchial cartilages, noting that they consist of a series of irregular cartilaginous plates. Note their arrangement around the wall of the bronchus. Observe the mucosa. What is the type of epithelium that forms the lining of the bronchus? Is there a well-defined basement membrane? Note the tunica propria, a layer of subepithelial connective tissue in which numerous scattered lymphocytes are to be seen. Find diffuse aggregations of lymphoid tissue; also small lymph nodules which may be present. Observe the muscular layer; does it form a complete or incomplete ring of smooth muscle fibers encircling the wall of the bronchus? Note the position of this muscular ring in relation to the bronchial cartilages. Identify the coarse collagenous and elastic fibers which form a thin layer between the muscular ring and the bronchial cartilages. Note that this layer can be traced between the cartilage plates and continues over their external surfaces. It thus appears that the external wall of a bronchus is a relatively thick layer of fibrous tissue into which, for its support, the cartilages have been inserted. Locate small groups of mucous glands. Note their position. What is their relation to the muscular layer? If possible find a duct which can be traced from these glands, through the muscular layer, to the surface of the epithelium. Note also that some of the glands are located in the tissue between the cartilages, with a few lying external to the cartilages. The fibrous tissue containing these glands can be compared with what layer in the wall of the alimentary canal? The ring of smooth muscle fibers is to be compared with what layer?

THE PULMONARY TISSUE

Identify one or two respiratory bronchioles, which are subdivisions of the terminal bronchioles. What type of epithelium lines these bronchioles? Are these cells ciliated? Note that a number of alveoli open into these bronchioles. What does this indicate concerning the function of these tubes? Do the terminal bronchioles have a respiratory function? Can you identify muscle fibers in the walls of the respiratory bronchioles? How do these bronchioles terminate? Identify the alveolar ducts, two or more of which may be seen branching out from a single respiratory bronchiole. Look for muscle fibers in the walls of the alveolar ducts. Note the number of alveoli which open into these ducts. Define and identify an atria. Observe the alveolar sacs. What type of tissue forms the walls of the sacs? Are muscle fibers present? Identify alveoli which open into the alveolar sacs and the atria.

Examine the walls of the alveoli with the high power. The oil immersion can also be used to advantage for this study. Can you verify the presence of an epithelial lining in the alveoli? Observe the capillary branches of the pulmonary artery, which are located between the walls of adjacent alveoli. Note the delicate connective tissue by which the capillaries are supported. Elastic fibers are abundant in this tissue, but can be demonstrated only by the use of special stains. Identify the septal cells (macrophages) in the connective tissue of the walls of the alveoli.

Examine a section of the periphery of the lung and identify the pleura. What type of cells form the lining of the pleura. Observe the thin layer of subepithelial connective tissue; does it contain any muscle fibers?

From your observations reconstruct a diagrammatic representation of the primary lobule of the lung, showing the distribution and relationships of the blood vessels to this pulmonary structure.

BLOOD SUPPLY OF THE LUNG. Examine a section of an injected lung with the low power. Note the position of the pulmonary vessels in the interlobular connective tissue; the smaller branches of these vessels which follow the divisions of the bronchioles in the lobules; the finely meshed capillary network between the adjacent air spaces.

Draw: showing the distribution of the pulmonary vessels and their relation to the pulmonary structures in the lungs.

METHOD OF IDENTIFICATION OF LUNG

Identification of lung tissue should offer the student no difficulty. *It is sometimes carelessly confused with bone marrow, but this is rather* inexcusable since bone marrow smears or sections are entirely cellular (small vessels or fragments of bone may be present) and there are no epithelial lined tubes such as are found in the lung and which are sections of the tubes of the bronchial tree.

STUDY OF THE URINARY SYSTEM

THE KIDNEY

Examine a kidney which has been sectioned longitudinally, the section passing from the curved lateral border through the renal sinus. The use of a hand magnifier will aid in identifying the parts of the kidney which may be observed in the section. Identify: the medial and lateral borders; the superior and inferior poles; the hilum, a deep notch in the medial border through which the renal artery enters and the renal vein and ureter leave the kidney. Note that the hilum is the entrance to a deep, baylike space almost completely surrounded by the substance of the kidney, the renal sinus. Observe the renal pelvis, which is the expanded upper portion of the ureter as it approaches the hilum. Note that in the renal sinus the pelvis divides into two or three membranous extensions, the major calyces. Each major calyx is subdivided into a number of smaller extensions, the minor calyces, into which the apices of the renal papillae project. Observe the division of the substance of the kidney into cortex and medulla. The medulla consists of a number of pyramids (renal or Malpighian pyramids). Note the manner in which the apex of each renal pyramid projects into a calyx. Occasionally two or more papillae may be found occupying the same calyx. Do any of the pyramids show a tendency to be lobulated at their bases? What does this signify? The cortex lies between the bases of the pyramids and the capsule. Note that portions of the cortex extend toward the renal sinus between the renal pyramids, the renal columns (columns of Bertini).

Examine the pyramids with a hand magnifier. Observe their striated appearance which is due to the presence and parallel arrangement of the collecting tubules which form the greater part of the medullary substance. Identify the medullary rays which are found by the continuation of the tubules from the pyramids into the cortex. (It should be borne in mind that in following the course of the urine through the tubules, it passes from the tubules in the cortical medullary rays to the tubules in the medulla.) The medullary rays, sometimes called the cortical rays, form the pars radiata of the cortex. The portion of the cortex between the rays is the pars convoluta or cortical labyrinth. Note the small granulelike bodies in the convoluted portion of the cortex. These are the renal or Malpighian corpuscles. Observe the capsule, which is a thin investing layer of fibrous tissue which is firmly attached to the surface of the kidney. Follow the capsular tissue into the renal sinus and note that it expands into the connective tissue which fills the space between the renal pelvis and the substance of the kidney. Note the manner in which this tissue surrounds and supports the renal vessels as they pass through the sinus. Identify these structures in a cross section of the kidney.

Draw: showing the structure of the kidney as it appears in gross section.

Examine the different parts of a section of kidney with the low power. Observe the renal pelvis. Note that its walls consist of a layer of transitional epithelium, a layer of subepithelial fibroelastic tissue, a layer of smooth muscle fibers arranged in longitudinally and circularly disposed bundles and an external layer of loose fibrous tissue (adventitia), which blends with the capsular connective tissue in the sinus. What is the relation of the calyx to the renal papilla? Note that the transitional epithelium becomes thinner as it passes from the renal pelvis into the calyx. Follow the epithelium as it is reflected from the wall of the calyx to the surface of the renal papilla. Observe the uriniferous tubules, noting their straight course in the medullary rays and the pyramids, as compared with the tortuous course of the convoluted arrangement of the tubules between the medullary rays, noting their relation to the renal corpuscles. Observe the cortical character of the tissue between the pyramids (cortical columns of Bertini).

Examine the cortex with the high power. Observe a renal corpuscle, noting that it consists of a series of closely coiled capillary loops, the glomerulus, which is enclosed by the two layers of Bowman's capsule. Identify the two layers of the capsule: the outer or parietal layer and the inner or visceral layer. Note that the visceral layer is closely applied to the loops of the glomerulus. The epithelial cells of both layers are quite thin, those of the inner layer being thinner than those of the outer layer. Identify the neck which connects the renal corpuscle with the proximal convoluted tubule. Note that it is a short tube, formed of flattened cells that enclose a narrow lumen. Identify the afferent and efferent arteries which enter and leave the capsule at a point called the vascular pole, which is opposite the neck. After entering the capsule the afferent artery breaks up into the capillary loops of the glomerulus.

Identify the proximal convoluted tubules. Note: the manner in which these tubules are grouped about the renal corpuscle; their narrow, somewhat irregular lumen, and that they constitute the greater portion of the pars convoluta. What is the shape of the cells that line the proximal convoluted tubules? Observe the shape and location of their nuclei. Notice that the darker basal portion of the cell has a striated appearance. What produces these basal striations? Note the lighter peripheral portions of the cells. Identify the brush border of the cells which give their free surface the appearance of being ciliated. Identify the distal convoluted tubules. They are fewer in number and located within the loops formed by the proximal tubules. Note that the cells which form their epithelial lining, are lower than those of the proximal tubules, the lumen of the distal tubule being correspondingly larger; the faintly marked basal striations; the absence of a brush border. Observe the arched (junctional) tubules; to be identified by the cuboidal form of their epithelial cells, their clear cytoplasm and deeply stained, spherical nuclei; the definite outline of the lumen. Observe the descending limbs of Henle's loop. Note their flattened epithelial cells; their large, oval nuclei; the bulging of the cytoplasm by which the nuclei are enclosed. Two or three nuclei may be seen in a single section of this portion of the tubule. Identify the ascending limbs of Henle's loop. Note their low cuboidal epithelial cells, with small spherical, deeply staining nuclei. Can basal striations and granules be observed in these cells? Four or five nuclei should be seen in a single section of this portion of the tubule. Note that the epithelial cells of all portions of the uriniferous tubules rest on a basement membrane which, although it is homogeneous in appearance, is fibrillar in structure. The connective tissue fibers, which are adjacent to the basement membranes of the tubules, are longitudinal in direction and form the external layer of the tubular wall.

It is essential that the normal amount of interstitial tissue should be carefully observed, since any considerable increase of this tissue indicates a pathological condition.

Draw a renal corpuscle surrounded by the proximal and distal convoluted tubules, the limbs of Henle's loop and the arched tubules.

Examine a section through the apex of a renal papillae with high power. *Observe the collecting tubules. Note the cuboidal cells which* form their epithelial lining; the clear cytoplasm of these cells; their deeply staining, spherical nuclei; their large, well-defined lumina. Identify the descending and ascending limbs of Henle's loops.

BLOOD SUPPLY OF THE KIDNEY. Examine a section of an injected kidney with the low power. Identify the cortex and the medulla, the latter being represented by the renal pyramids. Observe the large, interlobar vessels, noting their location between the cortical columns and the pyramids. If possible trace these arteries to their connection with the renal artery in the sinus. These arteries are branches of the renal artery. In their course between the pyramids, they follow extensions of the connective tissue from the sinus. Note that these connective tissue extensions form incomplete septa. Identify the arcuate *(arciform) arteries. Note their location in a narrow strip of connective* tissue between the basal portion of the pyramids and the cortex. Identify the interlobular arteries, they are branches of the arcuate arteries which extend perpendicularly toward the periphery of the cortex. Locate the afferent arteries (vasa afferentia) branches which pass laterally from the interlobular arteries to the glomeruli. Notice the glomeruli, capillary loops located within the capsules of the renal corpuscles. Identify the efferent arteries (vasa efferentia), small vessels through which the blood leaves the glomeruli. How does the size of an efferent artery compare with that of an afferent artery? What does this seem to indicate regarding the function of a glomerulus? Follow the branches of an efferent artery. To what are they distributed? Identify the arteriae rectae; follow their course to the medulla. They end in relation to *what structures?*

Draw: showing the distribution of the blood vessels (arterial) to the different structures in the kidney.

Examine a renal corpuscle with the high power. Observe: the inner and outer layers of Bowman's capsule; the capillary loops which form the glomerulus; the afferent and efferent vessels which convey blood to and from the glomerulus.

Draw: showing the glomerulus as it appears in relation to the structures of the capsule.

THE URETER

Examine a section of the ureter with the low power. Observe: the mucous coat, noting that it consists of an epithelium resting on a delicate subepithelial connective tissue; the muscular coat, noting the direction of the fiber bundles of the inner layer; their separation by intervening septa of connective tissue; the more definitely formed layer of circular fibers; the less scattered arrangement of the longitudinal bundles of the outer layer. The fibers of the outer layer, however, are not so compactly arranged as those of the middle layer. Identify the adventitia, a layer of loosely arranged fibroelastic tissue.

Draw: showing the appearance and structure of the ureter as seen in the section.

Examine a portion of the section with high power. Observe the form and arrangement of the cells of the epithelium which lines the ureter. Classify this epithelium. Observe the stroma, a subepithelial layer of connective tissue consisting of delicate fibers and having more or less the appearance of a reticulum. Note that numerous lymphocytes are present in this tissue. A narrow band of coarser fibers, sometimes called the submucosa, may be seen between the subepithelial connective tissue and the muscular coat. This layer is frequently absent and when present is distinguished with difficulty. Observe the muscular coat, noting that the inner bundles are somewhat scattered; the fiber bundles, in the middle of the muscular coat are more compactly arranged, while those of the outer layer are less compactly formed. Note that the third or external layer is more evident in the lower half of the ureter.

At the entrance of the ureters into the bladder, the circular fibers are considerably strengthened and form a sphincter which acts to keep the ureter closed except when urine is being discharged into the bladder.

Observe the loosely arranged fibers of the adventitia, noting that the fibers of this coat, which lies next to the muscular coat, are compacted to form a strong supporting structure for the outer wall of the ureter. Note, also, in this layer, blood vessels, nerves and small groups of ganglion cells.

Draw: showing the histological structure of the wall of the ureter.

THE BLADDER

Examine a section through the body of the bladder with the low power. Observe the epithelium. What type of epithelium lines the bladder? Note its thickness. How does it compare in this respect with the epithelium of the ureter? Note, also, the way in which it is folded to form pocketlike invaginations. Observe the subepithelial connective tissue. As in the ureter it consists of an inner part composed of delicate fibers and containing numerous lymphocytes, and a layer of considerable depth, composed of coarse fibrous tissue.

The tunica propria and the submucosa are not separated by a muscularis mucosae or some similar structure as in the alimentary canal, but gradually merge into one another, thus forming a stroma.

Small nodules of lymphoid tissue should be sought in the stroma; these are usually found in association with blood vessels. Small groups of ganglion cells may also be found in this layer. Observe the muscular coat, noting its exceptional thickness. *Although the wall of the bladder* consists of a considerable amount of fibrous tissue, the bladder is essentially a muscular organ. As far as possible, identify the three layers composing the muscular coat. These layers encroach on one another to such an extent that they are not clearly defined in sections. Examine the adventitia, a layer of loosely arranged fibrous and elastic tissue which forms the outer coat of the bladder. Is a serous membrane present? Note the blood vessels, nerves and small groups of ganglion cells which are present in this layer.

The connective tissue septa between the muscle bundles are extensions of the general connective tissue investment of the bladder. The blood vessels and nerves follow the pathways provided by these septa as they pass to the various structures in the wall of the bladder.

Draw a portion of the wall of the bladder showing its histological structure.

With a low power examine a section through the trigone. Follow *the above outline for observing its general structure. Identify the* crypts which are small, pocketlike invaginations of the epithelium. Note that some of these structures do not have a lumen, while others do. Is there any evidence of secretory activity on the part of the crypts in which a lumen is present? Note the greater complexity in the arrangement of the muscle bundles, also the increased thickness of the muscular coat. Note that the muscular tissue lies directly in contact with the subepithelial connective tissue; the submucosa, as observed in the section of the body of the bladder, being absent in the trigone.

Draw a portion of the trigone showing the histological structure of its parts; also the differences to be observed between it and the body of the bladder.

STUDY OF THE DUCTLESS GLANDS

The Thyroid Gland

Examine a section of the thyroid gland with the low power. Observe the follicles. Notice the variation in the shape and size of these structures which appear in the section as spaces enclosed by a cellular wall.

If possible, find follicles which are communicating with one another. Identify the capsule which consists of a thin layer of connective tissue which lies on the surface of the gland. Observe the septa, which are delicate connective tissue extensions of the capsule that enter the substance of the gland and divide it into primary and secondary lobules. Examine the interstitital (interfollicular) tissue. This tissue consists of loosely arranged fibers of connective tissue that extend from the capsule and fill the spaces between the follicles. Note that this tissue contains numerous blood vessels. In injected material you can see that the terminal capillaries form closely meshed capillary plexuses about the follicles. Observe the interfollicular cells which are cordlike masses of epithelial cells in the interstitial tissue. Note the extent to which these cell masses would resemble follicles if they were provided with lumina. Examine the colloid which is a homogeneous, hyaloid substance which stains with eosin (acidophilic), noting that it occupies the greater part of the space in the follicles.

Examine a portion of the same section with the high power. Observe several follicles and notice the height of the lining epithelial cells. Are the epithelial cells low or tall in an actively secreting follicle? In the section being studied are the cells of all of the follicles the same height? Explain this condition on the basis of the functional activity of the gland. Is there any correlation between size of follicle, quantity of contained colloid and height of the lining epithelium? Examine the interfibrillar spaces in the interstitial connective tissue. In the living condition these spaces are filled with a lymphlike fluid. Note that small amounts of colloid may be seen in some of these spaces. Identify the blood vessels in the interstitial tissue, noting the close relation of the smaller vessels to the follicular walls. Examine the colloid contained in the follicles. Note the vacuolated spaces between the colloid and the wall of the follicle. Are vacuoles, epithelial cells, droplets of mucus to be found in the colloid? Observe the masses of interfollicular cells. Do the cells of the follicular epithelium rest on a basement membrane?

Draw: showing the histological character of the structures observed in the thyroid.

THE PARATHYROIDS

Examine a section of a parathyroid first with low power, then with the high power. Observe the capsule, an investing layer of connective tissue in which a considerable quantity of fat may appear. Observe the epithelioid cells, closely packed into cords and masses. Note the wide sinusoidal spaces between the cell aggregations.

Identify the chief cells. These cells make up the greater proportion of the parenchyma. They may be recognized by their clear, nongranular cytoplasm, their relatively large, vesicular nuclei. Because the nuclei are relatively larger, these cells appear somewhat darker than the oxyphil cells. Identify the clusters of oxyphil cells. Note their eosinophilic cytoplasm, and their relatively small nuclei. Compare the absolute size of the nuclei of oxyphil cells with the nuclei of the chief cells. Note that the oxyphil cell is larger than the chief cell. Also note the increase in amount of cytoplasm of the oxyphil cell as compared to that in the chief cell. Observe the easily distinguishable cell outlines in the clusters of oxyphil cells. Notice also the variations in the sizes of these clusters. Observe the thin septa of connective tissue which surround the cell aggregations and support the sinusoids.

Draw: showing the histological structure of a parathyroid gland.

THE ADRENAL

Examine a section of the adrenal with the low power. Observe: The connective tissue capsule, and the division of the gland into cortex and medulla. Examine the sectioned surface of a freshly obtained adrenal, noting the difference in the color of the cortex and medulla.

Examine the section with the high power. In the cortex observe the cordlike arrangement of the epithelial cells. Look for the thin strands of fibrous tissue between the cords, noting that they are extensions of the capsule. Observe the division of the cortex into zones: (a) the outer zona glomerulosa, in which the cells present a spherical or coiled arrangement. What is the shape of the cells in the glomerular zone? What is the character of their cytoplasm? What is the form and appearance of their nuclei?; (b) the middle zona fasciculata, in which the cells are arranged in long, parallel columns. What is the shape of the cells in the columns? How many cells are included in the width of a column? What is the character of the nuclei of these cells? What observable characteristic of these cells explains the term "spongiocyte"?; (c) the inner zona reticularis, to be recognized by the reticulate arrangement of the cell cords; also by the darker color of the cells. Note the thin-walled sinusoids which occupy the meshes of this reticulum; note also how closely the endothelial lining of these sinusoids is applied to the cells of the cords.

Observe that the medulla occupies a position in the middle of the gland. Note the cell cords which form an irregularly meshed network adjacent to the zona reticularis of the cortex. Are the cords in the medulla continuous with those of the cortex? What form is assumed by some of the cells? How is this change of form to be accounted for? What is the characteristic color of these cells? What nervous elements can be identified in the medulla? Identify the large central vein through which the blood leaves the adrenal.

Draw: showing the histological structure of the adrenal as seen with the high power.

Examine a section of an injected adrenal with the low power. Observe the branches which form the vascular plexus in the capsule. Follow these branches as they pass downward between the cell columns from the capsule into the cortex. Note the capillary plexus about the glomerular zone; also the capillary network about the columns of the fasciculate zone. Observe the elongated meshes of this network. Identify the sinusoids between the network formed by the cell cords of the zona reticularis. Note the similar, but somewhat larger blood spaces between the cell cords in the medulla. Identify the large central vein which is located in the connective tissue in the middle of the medulla.

Draw, showing the vascular structures of the adrenal as seen in the section.

The Paraganglia

Examine a section of the carotid body with the high power. Observe its position in relation to the arteries. Identify the capsule, formed by a condensation of the connective tissue by which the body is surrounded. Examine the arrangement of its epithelioid cells in cords and masses, noting the manner in which they are separated by extensions of the connective tissue from the septa. Observe the relatively wide spaces occupied by the capillary sinusoids. Note the close relationship between the epithelioid cells and the capillary spaces. Also note that the rich vascular character of the body is indicated by the number of the vascular spaces and small capillary vessels in the capsule. Identify bundles of nerve fibers, noting that they are related to small groups of ganglion cells.

To distinguish between the chromaffin cells and the supporting cells, material should be used which has been treated with potassium dichromate, or another of the chrome salts.

Draw: showing the histological details of the section as seen with the high power.

The Hypophysis

Hold a section of the hypophysis to the light and examine it with a hand magnifier. Identify and note the difference in the size and appearance of the anterior, posterior and intermediate lobes. The anterior lobe will be seen to be cellular in structure, while the posterior lobe appears to be fibrous. The somewhat indefinite intermediate lobe may be recognized as epithelial lined spaces containing colloid, located between the anterior and posterior lobes.

Examine the section with the low power. Identify the anterior lobe (pars distalis). Note the fibrous tissue capsule that envelops the organ. The capsule is derived from the portion of the dura mater which forms the diaphragma sellae. Observe the arrangement of the cells in cords and masses between which are clearly defined vascular spaces, the sinusoids. Find aggregations of cells which resemble acini. Do these cell aggregations possess a lumen? Is there a substance contained in the lumen? Note the different staining properties of the cells. On the basis of their staining reaction, identify the acidophilic, basophilic and chromophobe cells. Which type appears to be the most numerous? Which type appears to be the least numerous? Can you make out any pattern of distribution of these types? Identify the pars intermedia. What types of cells are present in this area? Note the formation of follicles. What is the form and character of the cells of the follicular walls? Is colloid present in any of the follicles? Locate the narrow cleft (interglandular cleft) between the pars intermedia and the pars distalis. What is this cleft supposed to represent? With what kind of cells is it lined? Are any of these cells provided with cilia? If cilia are observed, how would their presence be explained? Examine the pars nervosa (posterior lobe). Note that it consists of fibrous tissue in which a number of irregularly shaped cells are present. In specially stained material these cells will be seen to be both stellate and fusiform in shape and to be provided with delicate protoplasmic processes. Their dark appearance is due to the fine pigment granules present in their cytoplasm.

Examine the section with high powers. Identify the different types of cells in the pars distalis. While these cells can be distinguished in hematoxylin and eosin preparations, the best results are obtained when special stains have been used. Observe: the alpha (acidophil) cells. These are the most numerous of the chromophil cells and may be recognized by the large, pink-staining granules in their cytoplasm: the beta (basophil) cells. These are the least numerous of the cells in the anterior lobe and may be recognized by their somewhat smaller, basophilic granules: the chief (chromophobe) cells. These cells are to be identified by their small size and their nonstainable, slightly granular cytoplasm. Note that the outlines of these cells are readily discernible. Observe and compare the nuclei of these three types of cells.

Draw a number of the cells observed, indicating their distinguishing characteristics and their relation to one another and to the sinusoids, as seen in the section.

In removing the brain from the skull, unless great care is exercised, the hypophysis becomes separated from the stalk, below the diaphragma sellae. For this reason the pars tubularis is not usually present in sections. When present its cells will be found to be predominantly of the chromophobe type, with their frequent arrangement in the form of follicles containing colloid.

THE PINEAL BODY

Examine a section of the pineal body with the high power. Observe its general form. Locate the stalk by which it was attached to the roof of the brain. Note the fibrous character of the stalk and the ependymal cells by which its cavity (pineal recess) is lined. Observe the capsule, consisting of fibrous tissue which is continued from the pia mater. Note the delicate septa extending from the capsule into the organ and dividing it into small, irregular lobules. Examine the cells which form the parenchyma of the pineal body. These are mainly of two types: small cells having a scanty cytoplasm and small, deeply staining nuclei, and larger cells with pale vesicular nuclei, the cytoplasm of which is reticulated or contains acidophilic or basophilic granules. Find cells which have assumed the form of small follicles and contain calcareous concretions (brain sand).

Draw: showing the histological structure of the pineal body.

STUDY OF THE SKIN AND ITS APPENDAGES

THE SKIN

With the low power examine a section of the skin from the palm of the hand. Observe the epidermis, noting its thickness; the ridges (crista cutis) into which its surface is moulded; the furrows (sulci cutis) between the ridges. Observe the subepidermal tissue, the corium. Identify the subcutaneous connective tissue, the tela subcutanea. Note the separation of the bundles of fibrous tissue in this layer, and the masses of fat cells which occupy the spaces between them. Observe the dermal papillae, which are moundlike, or fingerlike elevations of the corium projecting into the deep surface of the epidermis. Identify the sweat glands, long, slender, tubular structures which end in a number of coils in the deep part of the corium or in the tela subcutanea. Note the spiral formation of the ducts of these glands as they pass through the epidermis.

Draw: showing the general appearance and structure of the skin as seen in the section.

Examine a portion of the section with the high power. Observe the epidermis noting:

The stratum germinativum; its depth; its basal row of cylindrical cells (stratum cylindricum) which rests on a thin layer of reticular fibers (tunica propria); the succeeding layers of polyhedral cells; the separation of the cells in the intermediate layers; the delicate protoplasmic bridges which cross the intervening spaces and join the cells to one another; mitotic figures, which may be seen in the cells of some of the deeper layers of the stratum germinativum.

The stratum granulosum, consisting of three or four rows of spindle-shaped cells. Note its position in relation to the stratum germinativum; the deeply stained granules of keratohyalin, with which the cells are filled; the pale spherical nuclei.

The stratum lucidum, a narrow, colorless, apparently homogeneous layer between the stratum granulosum and the stratum corneum. By careful focusing and proper manipulation of the light the outlines of the cells in this layer can be made out. What are the shapes of these cells? Are the nuclei visible? Why are the outlines and cellular constituents of the cells in the deeper portions of the stratum corneum discernible, while those of the stratum lucidum are nearly or quite invisible?

The stratum corneum, extending from the stratum lucidum to the surface. Note that the cells, which are spindle-shaped at first, become increasingly flattened as they approach the surface on which they appear as thin, cornified scales.

The corium, noting its division into a papillary layer and a reticular layer. What is the difference in the histological structure of the two layers?

Examine the tela subcutanea, noting the wide separation of the bundles of fibroelastic tissue and the masses (lobules) of fat cells which occupy the spaces between them.

Identify Meissner's corpuscles in the dermal papillae; also Pacinian corpuscles in the subcutaneous tissue. The corpuscles can be best observed in sections of the skin from the tip of the finger.

Draw: showing the histological structure of the skin as observed in following the foregoing outline.

Examine an injected section of the skin with the low power. Observe the larger arteries passing through the tela subcutanea to the corium. Note the small vessels which form a network in the deep portion of the corium (subcutaneous plexus). Note, also, the network of smaller vessels just below the papillary layer (subpapillary plexus). Trace branches from the subcutaneous plexus to the secreting portions of the sweat glands and to the fat lobules. Also trace branches from the subpapillary plexus to the papillae, in which they form capillary loops. Is there any difference in the blood supply to a papilla in which a Meissner's corpuscle is located and one in which a corpuscle is not present?

Observe two or three sweat glands with the high power. Note: the coiled, secreting portion of the gland located in the deep part of the corium or in the loose areolar tissue below the corium; the cuboidal, or columnar cells with which this portion of the gland is lined; the small, spindle-shaped cells between the secreting cells and the basement membrane. How is the basement membrane to be recognized? What is to be observed in the cytoplasm which indicates the secretory character of these cells? Follow the duct, of which only fragments can be seen here and there, through the corium and the epidermis. How many layers of cells are included in its wall? What is the difference between the course pursued by the duct in the corium and in the epidermis? At what point on the surface of the skin, does the duct open?

Draw: showing the histological structure of a sweat gland.

For the distribution of elastic fibers in the skin see areolar tissue (p. 53).

THE HAIR

With the low power examine a longitudinal section through the scalp. Observe the epidermis. Compare the thickness of the epidermis of the scalp with that of the palm. Examine the corium; note that both the corium and the tela subcutanea are considerably thinner here than in those areas which are subject to pressure.

Identify the hair follicles. Owing to their oblique position in the scalp, a longitudinal section of an entire follicle will probably be impossible to find, therefore, it will be necessary to study several follicles cut at different levels in order to understand the structure of a single follicle. Identify the sebaceous glands, noting that their ducts open in the region of the neck of the follicle.

Select a follicle, sectioned through the level in which the structures called for can best be identified, and examine with the high power.

Follow the epidermis as it is continued into the follicle. What is the extent of the stratum germinativum in the follicle? What part of the follicle does it form? How far into the follicle does the stratum corneum extend? Can the stratum granulosum be identified? What is its extent in the follicle?

Observe in the middle third of the typical follicle:

The theca, a capsulelike arrangement of the connective tissue surrounding the follicle. Identify: an outer layer of longitudinal fibers which is sometimes called the vascular layer, owing to the number of blood vessels it contains; an intermediate, somewhat thicker, layer of circularly arranged connective tissue fibers; a narrow, inner layer of clear, homogeneous material, the hyaline membrane.

The outer root sheath, continuing the stratum germinativum of the epidermis. Follow this layer into the enlargement at the end of the follicle, the bulb.

The inner root sheath; identify: an outer layer of somewhat flattened cells in which the nuclei are more or less indistinct, Henle's layer; a middle layer of one or two rows of colorless, cuboidal cells in which the nuclei are more apparent, Huxley's layer; an inner layer of cornified cells, arranged so that they overlap one another, the cuticular layer of the inner root sheath.

The hair shaft or hair proper, consisting of the hair cuticle, which is so closely applied to the cuticle of the inner root sheath that the two have the appearance of a single structure. Identify the cortex, composed of elongated, spindle-shaped cells closely packed together and forming the greater part of the hair shaft; the medulla, a central core of cells which show marked evidence of degeneration. The medulla is not present in all hairs, and not always present in different parts of the same hair.

The bulb; note that the theca is continuous with the papilla on which the bulb rests; that the hyaline membrane is continued over the papilla between the connective tissue and the epithelial cells; that the outer root sheath is continued about the bulb as a single layer of cuboidal cells and over the papilla as a layer of columnar cells; that the inner cells of the outer root sheath and the layers of the inner root sheath merge in an undifferentiated mass of epithelial cells in the bulb. This mass of undifferentiated epithelial cells forms the matrix. Follow the cells of the matrix as they pass upward to form the cortex and medulla of the hair shaft.

Draw: showing the histological structure of a hair-follicle as seen in longitudinal section.

With the high power, examine a section of the scalp in which the hair follicles can be studied in cross section.

It will be noted, in studying cross sections of the hair follicles that many of the sections represent different levels of the follicles. For this reason cell layers which can be identified in some sections are not to be seen in others.

Find a section in which all of the cell layers which have been identified in the previous study can be observed. In the hair shaft identify the medulla, the cortex and the hair cuticle. In the inner root sheath identify Huxley's layer; Henle's layer. Observe the outer root sheath. Identify the theca, noting the hyaline membrane; the inner, circular layer of connective tissue fibers; the outer longitudinal layer of connective tissue fibers and the blood vessels which it contains.

Find a section through the neck of a follicle and examine with the high power. (A section through this level can be identified by the presence of the sebaceous glands.) What cell layers in the hair shaft and root sheaths are not present in a follicle sectioned at this level, which were identified in the foregoing sections?

Find a sebaceous gland that can be followed to its connection with a hair follicle. Examine with the high power. Observe that the gland is an outgrowth of the epithelium of the wall of the follicle. Note its saccular form. Note that the epithelium of the duct of the gland is several layers of cells in thickness, continuing the stratified squamous epithelium of the outer root sheath. However, it is soon reduced to a single layer of cuboidal or low columnar cells from which the cells of the body of the gland are derived. What are the histological differences between the cells of the external layer and those contained in the body of the gland? Note: the transformation of these cells as they produce the substance secreted by the gland: *small cells newly formed by division from the epithelial cells of the basal layer of the gland; larger cells, with definitely formed nuclei, in which small fat droplets are beginning to appear;* cells in which the nuclei have become obscured by the increase of fatty material in the cytoplasm (the fading of the nucleus may be interpreted as a part of the degeneration of the cell); cells in the process of disintegration. The oily substance or sebum into which the fat droplets have been transformed is released by the disintegration of these cells. This takes place in or near the duct through which the sebum passes into the follicle.

Draw: showing the histological structure of a sebaceous gland.

THE NAIL

Hold a longitudinal section of a nail to the light and with a hand magnifier identify the following: the portion of the terminal phalanx by which the tip of the finger is supported; the nail plate (nail). The body of the nail lies in front of and its root lies beneath the nail fold. Note that the root lies between two *epithelial layers, the epithelium of the nail bed and the inverted epithelium of the nail fold. Thus it* may be said to lie in an epithelial groove—the nail groove. Observe the nail bed, the tissue on which the body of the nail rests. The full extent of the nail bed is from the body of the nail to the bone.

Examine the section with the low power. Observe the epidermis covering the tip of the finger. Note: the stratum corneum; the stratum granulosum; the stratum germinativum; also the number and size of the papillae by which the epithelium is penetrated. Note the changes that take place in the epidermis as it is continued over the tip of the finger and extends beneath the nail plate. The stratum germinativum becomes thinner, *the stratum granulosum, the stratum corneum and the dermal papillae disappear. Note that the matrix is considerably thicker than the portion of the epithelial tissue on which the body of* the nail rests. Note also *the presence of papillae in relation to the matrix* and the manner in which the cells are modified adjacent to the root of the nail. Apply the same observations to the cells of the *matrix* in which the root of the nail ends. Observe the infolding of the epidermis above the root of the nail to form the nail fold, noting that its stratum corneum rests on the upper surface of the nail plate. A thin layer of the stratum corneum will be seen extending from beneath the nail fold—the eponychium.

An extension of the stratum corneum may be seen beneath the free edge of the nail, especially in very young children—the hyponychium.

Examine a cross section of a nail with the low power. Observe the fold of skin which forms the nail wall on either side of the nail plate. Identify the nail grooves, deep recesses beneath the nail walls in which the borders of the nail plate rest. Follow the continuation of the stratum germinativum beneath the nail plate to form the epithelial portion of the nail bed. At what point does the stratum granulosum end? Observe the portions of the stratum corneum on each border of the nail, forming the lateral extensions of the eponychium. Note the papillated appearance of the epithelial portion of the nail bed.

In the longitudinal section of the nail the dermal papillae are to be seen in relation to the matrix, but not in relation to the epithelial tissue in front of the matrix. Papillae are present in the epithelium beneath the body of the nail in the cross section. Explain.

Using the high power, observe the flattened, cornified cells of which the body of the nail is composed.

Draw: showing the histological structure of the nail as seen in cross section.

THE MAMMARY GLAND

THE INACTIVE PHASE. Using the low power, examine a section of the mammary gland of a young nulliparous female. Observe the small, undeveloped alveoli, noting that the glandular elements are scattered, being widely separated by the surrounding connective tissue. Note the broad septa of connective tissue which separate the lobules, noting that the lobules are imperfectly outlined. Observe portions of the lactiferous ducts which may be seen passing from the lobules into the interlobular septa.

Draw: showing the general appearance of the section.

Examine a single lobule with the high power. Observe the ducts and their branches which end in slightly expanded extremities (alveoli) or in masses of epithelial cells in the form of solid cords. Examine a cross section of an alveolus, noting: its clear, narrow basement membrane; the double layer of cells indicated by two rows of nuclei. What is the shape of the cells of the inner row?

Identify the myoepithelial elements. What is the shape of these cells? Where are they located? Note that the myoepithelial cells do not form a continuous layer.

Observe the epithelium of the ducts. What is the shape of the epithelial cells lining the smaller ducts? The epithelial cells lining the larger ducts are what shape? The lactiferous ducts, which are to be seen only in special sections, are lined by a stratified columnar epithelium. Can you identify a basement membrane beneath the epithelium of the ducts? Note that the wall of the duct is completed by a condensation of the adjacent connective tissue fibers, which are arranged longitudinally.

Note, also, that the myoepithelial elements are more abundantly present about the walls of the ducts than about the alveoli. What is the reason for this? Observe the predominance of connective tissue in the structure of a lobule. Numerous lymph spaces are to be observed in this tissue. In specially prepared material a variety of cells, mostly phagocytic, can be demonstrated. Why are mast cells abundant in the tissue of the mammary gland? Name another place where mast cells are also abundant. Is there any similarity in these localities which might be suggestive of the functional character of the mast cells? Observe the alveoli. When they can be identified, these structures are to be seen as small, collapsed, or cordlike structures at the ends of the smaller ducts. Occasionally a small, expanded alveolus may be found in which a quantity of albuminous secretory material (colostrum) is present. Notice the masses of adipose tissue which appear throughout the section. Is the adipose tissue to be found in the immediate neighborhood of the glandular structures?

Draw: showing the histological structure of the alveoli and ducts, and of the surrounding tissue.

THE ACTIVE PHASE. Examine a section of a lactating mammary gland with the low power. Observe the lobules, noting the increase, both in the number and size, of the alveoli. The alveoli are greatly expanded by the amount of secretion they contain. Examine the interstitial tissue, noting that it has been reduced to thin septal partitions by the growth and expansion of the alveoli.

Draw: showing the general appearance of the section.

Examine a few of the alveoli with the high power. Observe the low columnar or cuboidal cells which line the alveoli. Note that some of the secreting cells, in which droplets of fat can be seen, are pyramidal in form. Note, also, the position of the spherical or oval nuclei in the basal portions of the cells. Observe the secretory product of the gland. Note that it differs from the colostrum (cf. inactive phase) in the number of fat droplets it contains. Note, also, the deeply stained nuclei which indicate the presence of leucocytes in the secretion.

Draw: showing the arrangement and histological structure of the alveoli of a lactating gland.

METHOD OF IDENTIFICATION OF MAMMARY GLAND

Students sometimes have difficulty in distinguishing between thyroid gland and a lactating mammary gland. This difficulty can be quickly cleared up if the student will remember that the mammary gland is an exocrine gland and, therefore, has a system of epithelial lined ducts, while the thyroid gland, which is an endocrine gland, has no duct system. Therefore, in differentiating these two structures the duct system, or lack of it, furnishes an important key.

STUDY OF THE MALE REPRODUCTIVE ORGANS

The Testis

Examine a section in which the testis can be seen in relation to the structures of the scrotum. Sections through the testis and scrotum shortly after the descent of the testis has taken place is instructive material for this study.

Hold the section to the light and with the use of a hand magnifier, observe the testis and note its position in relation to the surrounding structures. Observe the space (serous cavity) between the testis and the wall of the scrotum. Note that this space lies between the two layers of a saclike extension of the peritoneum (processus vaginalis). Examine the septula testis which are connective tissue partitions that divide the cavity of the testis into compartments or lobules. Observe: the seminiferous or convoluted tubules, coiled tubules which occupy the space included in the lobular compartments; the epididymis, a body, formed by densely compacted fibrous tissue and tubules, posterior to the body of the testis. If the section is cut longitudinally the head (globus major), the body and the tail (globus minor), can be distinguished. Identify the vas deferens, a thick-walled tube which is closely associated, by position, with the coils of the ductus epididymis in the globus minor. Examine the wall of the scrotum extending from the testis to and including the integument.

Examine the section with the low power. Observe: the integument, noting the thinness of its epidermal layer; the hair follicles; small sebaceous and sweat glands. Can you identify bundles of smooth muscle fibers intermingling with the fibers of the subcutaneous tissue? The stratum in which the fibrous tissue and smooth muscle fibers are intermingled is known as the dartos. The area between the dartos and the testicle is occupied by tissue which is derived from the abdominal fascias. Identify the cremasteric fascia. It consists of a layer of fibrous tissue containing scattered bundles of striated muscle fibers. With what layer of the abdomen is it continuous? Identify the tunica vaginalis. It is a delicate membrane consisting of flattened mesothelial cells supported by a substratum of delicate connective tissue. Note that the tunica vaginalis presents two layers: a parietal layer, which lines the inner surface of the scrotal sac, and a visceral layer which lies upon the surface of the testis. If a cross section is being studied, note the extent of the serous cavity. Between the cremasteric fascia and the parietal layer of the tunica vaginalis is a thin layer of cremasteric fascia which is derived from what abdominal fascia?

Identify the tunica albuginea which is the firm, fibrous outer wall of the testis. Follow extensions of this layer into the substance of the testis. Do these extensions or septa form complete partitions? What is the shape of the compartments formed by these septa? What are the structures which fill these compartments? Observe sections through the *seminiferous tubules, noting the germinal epithelium which forms their* lining. Identify the mediastinum testis, showing a network of cleftlike spaces, the rete testis. Note the irregular form of the rete testis; the flattened epithelial cells by which it is lined. Where is the mediastinum located in relation to the testis? *Identify the straight tubules (tubuli recti)* which connect the seminiferous tubules with the rete testis. Note that some of the straight tubules lie in the septula. What changes in the form of the epithelium are to be observed in passing from the seminiferous tubules to the straight tubules? Identify the epididymis. Note the groups of sectioned tubular structures which appear in the head of the epididymis; some are efferent ducts, which can be identified by the wavy outline of their epithelium, while others represent the duct of the epididymis. The ductus epididymis can be distinguished by the regular outline of its epithelium. In the longitudinal sections the duct of the epididymis can be traced to the tail, in which sections of the vas deferens can be seen.

Draw: showing the relationships and general histological appearance of the structures observed in the section.

THE SEMINIFEROUS TUBULES

With the high power examine a section of the seminiferous tubules which has been stained with Heidenhain's iron hematoxylin and counterstained with eosin. Observe the walls of the tubules, noting that they consist of closely interwoven fibrous tissue. With the use of selective stains (Verhoeff's elastic tissue stain) the presence of a considerable amount of elastic tissue can be demonstrated. Observe the germinal epithelium which forms the lining of the tubules. *Identify the spermatogonia*, which are cuboidal or spherical cells containing small, spherical, densely chromatic nuclei. Note that these cells rest on a thin basement membrane. Identify the spermatocytes, large cells which have large, vesicular nuclei. The chromatin pattern in the nuclei of these cells may vary from a spireme to definitely formed chromosomes. Observe the secondary spermatocytes, cells about half the size of the primary spermatocytes, having small, densely chromatic, spherical nuclei. Identify the spermatids, small cells with densely chromatic nuclei which form the several layers that line the lumen of the tubule. Spermatozoa are to be recognized by their deeply stained, conical heads and long *filamentous tails. As a rule, the heads of the spermatozoa* are embedded in the sides of the cells of Sertoli, their tails extending into the lumen.

Identify the cells of Sertoli; their position is indicated by their large, pale, vesicular nuclei containing well defined nucleoli: their outlines being masked by the cells which surround them.

Draw: showing the histological characters of the cells lining a seminiferous tubule.

Spermatozoa usually pass as rapidly as they are freed from the cells of Sertoli, from the seminiferous tubules into the epididymis. For their study it may be necessary to wait until the tubules of the epididymis are being examined.

Using the high power objective, examine one or two groups of interstitial cells. Note their size, shape, nuceli. What are the characteristics of the nuclei? Is more than a single nucleus present in any of the cells observed? How many nucleoli are present in the nuclei? What is the character of the cytoplasm? Do these cells produce a hormone? If so, what is it called and what is its effect?

Draw: showing the structure of the interstitial cells

THE SPERMATIC DUCTS

EFFERENT DUCTS AND EPIDIDYMIS

Using the low power examine a section passing through the head (globus major) of the epididymis. Observe that two kinds of tubules are present in the section, those in which the epithelium has a wavy appearance (efferent ducts), and those in which the epithelium is regularly formed (ductus epididymus). Observe the fibrous interstitial tissue containing blood vessels and nerves.

Examine the section with the high power. Observe the epithelium forming the lining of the efferent ducts. Note that the tall, columnar cells alternate with cuboidal cells, giving the epithelium an irregular, wavy appearance. The cuboidal cells give the impression of glandular depressions in an otherwise columnar epithelium. Note the cilia on the free surfaces of the columnar cells. Are cilia present on any of the cuboidal cells? Note, also, the delicate basement membrane on which the epithelium rests; the thin layer of circularly arranged smooth muscle fibers external to the basement membrane; the fibrous tissue, containing blood vessels, nerve fibers and small ganglion cells, by which the ducts are surrounded and supported. Observe the epithelium of the ductus epididymidis. Note the small, round cells which form the basal layer; the tall, columnar cells of the superficial layer; the flame-shaped clumps of cilia (stereocilia) which are borne on the free surfaces of the columnar cells; the thin basement membrane on which the basal cells of the epithelium rest; the layer of circularly arranged smooth muscle fibers external to the basement membrane. Observe the small ganglion cells associated with the muscular layer which, together with a plexus of delicate fibers from the sympathetic system, form the plexus myospermaticus. Are any spermatozoa to be seen in the duct of the epididymis?

Draw a few of the tubules of both the efferent ducts and the duct of the epididymis, showing their histological structure.

THE VAS (DUCTUS) DEFERENS

Examine a section of the vas deferens with the low power. Observe the mucosa which consists of an epithelium and a subepithelial layer of connective tissue. Observe, also, the muscularis, a thick layer of smooth muscle fibers external to the subepithelial connective tissue. Examine the adventitia, a layer of fibrous tissue in which elastic fibers are abundantly present. This layer merges with the fibrous tissue of the cord.

Draw: showing the general appearance of the vas deferens as seen with the low power.

Examine the section with the high power. Observe the epithelial lining of the vas. Note that it consists of two layers of cells—a basal layer of small, rounded cells, and a superficial layer of columnar cells. Compare the epithelium of the vas with that of the duct of the epididymis.

The epithelium of the vas deferens, just before it joins the ejaculatory duct, frequently develops several layers of cells and resembles the transitional epithelium of the prostatic portion of the urethra. There is also considerable variation in the way the cilia are distributed in the vas. In some cases they are found throughout the length of the duct; in others cilia are present only in scattered areas and not infrequently may be absent altogether.

Observe the subepithelial layer consisting of fibroelastic tissue, the elastic fibers predominating. Examine the muscularis consisting of three layers of smooth muscle fibers; those of the inner layer are arranged in scattered, longitudinal bundles; those of the middle layer are circularly arranged and those of the outer layer are also longitudinally directed. Identify nerve fibers and groups of small ganglion cells associated with the fiber bundles of the muscularis, and forming the plexus myospermaticus. Observe the adventitia, an external layer of loosely arranged fibroelastic tissue. Identify the blood vessels and small bundles of nerve fibers in this layer. Note the folds into which the mucosa is raised.

Sections through the vas deferens at different levels should be studied for the purpose of observing the manner in which the mucous membrane is raised into a series of folds. These elevations are broad and low in the proximal portion of the vas. They become higher and narrower toward the distal end until, in the ampulla, they develop secondary and tertiary folds which anastomose and form what is known as an alveolar surface.

THE SPERMATIC CORD

Examine a section through the spermatic cord with the low power. Observe the vas deferens, noting that its position is posterior to the other structures of the cord. Study the vas, following the preceding outline. Note the scattered bundles of striated muscle fibers, representing the cremasteric fascia. Identify the spermatic arteries and the sections of the veins belonging to the pampiniform plexus. Identify, also, small bundles of nerve fibers representing the spermatic nerves. Occasionally it is possible to identify the serous and fibrous portions of the processus vaginalis in the spermatic cord. Note the loosely arranged fibrous tissue by which the various structures of the spermatic cord are bound together.

Draw: showing the structure of the spermatic cords as seen in the section.

THE ACCESSORY GLANDS

SEMINAL VESICLES

Examine a section of the seminal vesicles with the low power, using the high power for verifying the more minute details of structure. Observe the larger divisions of the vesicles formed by the saclike diverticula. Note the fibromuscular tissue of the septa between the diverticula. *Observe the numerous thin folds into which the mucosa is* raised. Note: the secondary and tertiary folds; the recesses or crypts which they enclose. Identify the thin layer of circularly arranged smooth muscle fibers surrounding the walls of the diverticula. In the wider septa small, scattered bundles of longitudinal smooth muscle fibers should be looked for. These will be found, if present, external to the circular fibers. Identify the groups of small ganglion cells—the plexus myospermaticus—which may be seen in the connective tissue between the muscle bundles. These nervous elements are best observed in specially stained sections.

Draw: showing the general appearance (low power) and histological structure (high power) of a seminal vesicle as seen in the section.

THE PROSTATE GLAND

Hold a section of a prostate gland to the light and examine with a hand magnifier. Observe the thin, densely compacted, fibrous capsule by which the prostate is invested. Identify the median septum, appearing as a broad partition of fibrous tissue in the middle portion of the section. Examine the prostatic urethra, noting its crescentic form, which is due to the thick conical ridge (colliculus seminalis) projecting into it from its dorsal wall. It will be observed that the medium septum forms a thick, fibrous ring about the urethra, and that this ring is penetrated by the ducts of the glandular tissue of the prostate. Observe the *connective tissue septa, extending from the median septum to the capsule* and dividing the prostate into a number of compartments—the lobules of the gland. Study the glandular tissue of the prostate. Follow the ducts from the median septum into the lobules. Note the manner in which they branch and that the branches end in expanded tubules or alveoli. It will be seen that the tubules in each compartment or lobule converge to form a single duct, although a single duct may convey the secretion from two or more lobules to the urethra. Trace, if possible, the course of a duct to its connection with the urethra.

Draw: showing the structural character of the prostate gland, as seen in the section.

Examine the glandular structure of the prostate with the high power. Observe the epithelium forming the lining of the ducts. Note the manner in which it varies, being a simple columnar epithelium in some places and a two layered stratified columnar epithelium in others. As the duct approaches the urethra, the epithelium changes to the transitional type. Observe the secreting structures of the gland. Follow the course of one of the ducts into the lobule. Note the manner in which it divides into a number of branches; the saccular expansions (terminal tubules, or alveoli) in which the branches end. Similar expansions occur along the course of the duct, forming the duct alveoli. The epithelium which lines the alveoli differs little from that which lines the ducts, varying from a simple columnar to a two-layered or three-layered epithelium. Identify the interstitial tissue or stroma, fibromuscular tissue which extends from the septa into the lobules and binds the alveoli together. Observe the blood vessels. Note that the larger vessels are located in the septa, their smaller branches passing into the interstitial tissue and forming capillary networks about the alveoli. Identify the prostatic concretions or amyloid bodies. Masses of starchy (see iodine reaction) material laid down in concentric layers in the larger alveoli. While these concretionary bodies may appear in the prostate at any time, they are most commonly found in the prostates of elderly subjects.

Draw: showing the histological structure of the prostate as seen with the high power.

Examine a section through the prostatic portion of the urethra with the high power. Observe the crescentic form taken by the urethra as it bends over the thickened portion of its dorsal wall, the colliculus seminalis or crista urethrae. Examine the furrowlike extensions of the urethra on the sides of the colliculus, forming the prostatic sinuses. Identify the transitional epithelium which forms the lining of the urethra. Note that the epithelium is of the stratified columnar type in the prostatic sinuses. Identify the utriculus, a tubular structure representing the lower end of the Müllerian duct (uterus masculinus). This tube extends dorsally in the prostate for a variable distance and frequently ends in an expansion in the region of the "middle lobe." In the section it appears as a slitlike opening located at the summit of the colliculus. In sections in which the utriculus does not open into the urethra, it can be recognized as a tubular structure, between the two ejaculatory ducts, *which is lined by a two-layered stratified columnar* epithelium. Identify the ejaculatory ducts, tubular structures which may be identified by their position on either side of the utriculus and by their epithelium, which is similar to that lining the urethra. Note that the irregularity of their walls is caused by the ridges or folds into which the mucosa of the ducts is raised. Observe the numerous, thin walled vascular spaces, which give the colliculus the appearance of being supported by erectile tissue.

The vascular spaces are subdivisions of the vessels brought into the colliculus with the ejaculatory ducts. When these spaces are dilated by an inflow of blood, the colliculus becomes swollen and closes the urethra, thus preventing the flow of the semen into the bladder.

Observe the urethra. Note that its wall consists of a lining of transitional epithelium, except in the prostatic sinuses (see above); a subepithelial tissue, filled with a plexus of venous vessels, which give this portion of the wall the appearance of erectile tissue; a muscular coat, consisting of smooth muscle fibers arranged in an inner longitudinal layer and an outer circular layer. External to the muscular coat the wall of the urethra is continuous with the fibromuscular stroma of the prostate gland.

Draw: showing the histological structure of the colliculus and the prostatic urethra.

THE BULBOURETHRAL (COWPER'S) GLAND

Examine a section of a bulbourethral gland with the low power. Observe the fibromuscular capsule noting that striated, as well as smooth muscle fibers are present. Note the continuation of the fibromuscular tissue of the capsule into the gland to form the stroma by which the small lobules, consisting of groups of alveoli, are outlined; the mucus-secreting character of the cells lining the alveoli and ducts.

Using the high power, examine a section of a single alveolus. Observe the wide lumen. Note the clear, mucoid appearance of the cytoplasm; the basally located nuclei; the deeply stained (acidophilic) bodies or inclusions which are to be seen in some of the cells.

Draw: showing the histological character of an alveolus.

The Penis

Hold a section of the penis to the light and examine with a hand magnifier. Identify the three cylindrical bodies, the paired corpora *cavernosa, and the single corpus spongiosum.* Observe *the tunica albuginea*, which is a fibrous sheath that appears as a thick ring of densely compacted fibrous tissue surrounding the corpora cavernosa and the corpus spongiosum. Note the extension of this sheath between the corpora cavernosa—the median septum. Observe the skin which forms the external covering of the penis. Note the numerous, irregular vascular spaces in the corpora cavernosa and corpus spongiosum—the erectile tissue of the penis. Identify the slightly curved, slitlike opening in the corpus spongiosum that is the penile portion of the urethra.

Examine the section with the low power. Observe the skin, noting: *the thin epidermis; the subepidermal tissue or corium containing a few small sebaceous and sweat glands.* Examine the layer of subcutaneous *connective tissue between the skin and the tunica albuginea.* Note that it contains small bundles of smooth muscle fibers and has somewhat the character of the dartos of the scrotum. Also identify blood vessels and nerves in this layer. Observe the tunica albuginea, the densely compacted fibrous tissue sheath. Note that the fibers form an outer longitudinal layer and an inner circular layer. The median septum is seen as an extension of the tunica albuginea between the corpora cavernosa. From sections of the penis taken a short distance behind the glans penis, the median septum is incomplete; neither the septum nor the tunica albuginea extend into the glans. Note that the albuginea about the corpus spongiosum is thinner and not so firmly woven as that about the corpora cavernosa. Examine the erectile tissue, the principal tissue of the corpora cavernosa and corpus spongiosum. Note the fibromuscular trabeculae between the irregular blood spaces or lacunae. The lacunae are larger and the trabeculae are thinner in the central than in the peripheral portions of the corpora cavernosa. Observe the lacunae and trabeculae of the corpus spongiosum, noting that the lacunae are smaller and that the trabeculae are thicker than in the corpora cavernosa; the urethra, noting its position and the type of epithelium lining it. Observe any changes in the character of the epithelium in the penile portion of the urethra.

Draw, showing the histological structure of the penis as seen in the section.

Examine the tissue surrounding the urethra with the high power. Identify the saccular outpocketings which may be seen here and there—the lesser glands of Littré. What type of epithelium lines these glands? Locate and study the branched tubular glands which are connected with the urethra by ducts—the greater glands of Littré. Note the type of epithelium by which the secreting portions (alveoli) of these glands are lined. From the appearance of the epithelial cells, what appears to be the nature of the substance secreted by these glands? Observe the subepithelial tissue or stroma. Note the thin-walled venous spaces which it contains and its similarity to the erectile tissue of the corpus spongiosum.

External to the stroma a thin layer of circularly arranged smooth muscle fibers may be present on the lateral and dorsal sides.

Draw: showing the histological structure of the penile portion of the urethra.

STUDY OF THE FEMALE REPRODUCTIVE ORGANS

THE OVARY

Hold a section of an adult ovary to the light and examine with a hand magnifier. Observe the form and size of the section. Identify the cortex and the medulla. Note the difference in their staining reactions. What is the relation of the cortex to the medulla? Identify several Graafian follicles which appear as large, clear spaces enclosed by a zone of deeply staining cells. Identify the broad ligament, which is a band of connective tissue to which the ovary is attached.

Examine the section with the low power. Observe the manner in which the connective tissue of the broad ligament is continued into the ovary and forms the stroma of the medulla. Examine the tunica albuginea. It is a layer of connective tissue at the periphery of the cortex, in which the fibers are more regularly arranged and more densely compacted than in the remainder of the cortical stroma. Identify the germinal epithelium; a layer of cuboidal cells resting on the tunica albuginea. Note that this layer has the appearance of being a continuation of the peritoneal covering of the broad ligament. As age advances, the cells of the germinal epithelium become flattened and are more difficult to distinguish from the mesothelial cells of the broad ligament. Locate the primary follicles; note their number in the peripheral portion of the cortex. Each primary follicle consists of one or two layers of flattened epithelial cells (mantle cells) surrounding the large egg cell or ovum. Examine the Graafian follicles. They are seen as large spaces in the stroma of the cortex, enclosed by a wall which is composed of several layers of epithelial cells, the stratum granulosum. In mature follicles the ovum may be seen embedded in a heaped-up mass of epithelial cells, the cumulus oöphorus. Identify a corpus luteum which may be recognized by the arrangement of the epithelial cells in a series of folds. It may also appear to be slightly yellow in color. Identify a corpus albicantia, to be recognized by its hyaline appearance and irregular outline. Examine the more lightly stained and more loosely arranged fibrous tissue of the medulla. Note the many blood vessels it contains.

Draw: showing in detail, the general structure of the ovary.

Using the high power examine a section of the ovary of one of the smaller animals. Observe a primary follicle in the peripheral portion of the cortex. Note that each follicle consists of an ovum surrounded by a layer of flattened, epithelioid cells; its large, vesicular nucleus containing a scanty network of chromatin. Examine a follicle in which the epithelioid cells surrounding the ovum have become more or less cuboidal and have multiplied to form two or three superimposed layers. Note, also, that the connective tissue about the follicle has assumed a more regular arrangement and forms the theca folliculi. Examine a follicle in which the cells of the follicular epithelium have multiplied and form a number of cell layers about the ovum. In follicles of this stage note the beginning of the antrum, in the form of one or more clefts between the cells of the stratum granulosum. Find a mature follicle and observe the following: the antrum or spaces containing the follicular fluid (liquor folliculi); the stratum granulosum, consisting of several superimposed cell layers forming the wall of the follicle; the theca folliculi, which is a condensation of the connective tissue immediately about the follicle. Note the difference in the structure of the fibrous theca externa and the vascular (inner) theca interna. Observe the cumulus oöphorus, the heaped-up mass of epithelioid cells containing the ovum. Note the layer of tall, columnar cells, forming the corona radiata about the ovum; the thick membrane forming the cell wall of the ovum, the zona pellucida.

Draw: showing each stage in the development of a Graafian follicle.

Examine sections through ovaries in which the corpus luteum, the corpus hemorrhagicum and the corpus albicans can be observed.

THE CORPUS LUTEUM. Note the arrangement of the wall of the follicle in more or less definite folds. Observe a small group of lutein cells. Note their form, modified by mutual pressure in the mass; their small, eccentrically placed nuclei. Is there any indication of the presence of lutein pigment in these cells? What evidence is there that they may contain fat droplets?

THE OVIDUCT

Using low power, first examine the sections of the oviduct for their general appearance and the relation of their parts. Shift to high power and examine a small segment of the wall for histological details.

THE ISTHMUS. Examine a section of the isthmus. Examine the mucosa. Classify the type of cells lining the lumen. Are any of these cells ciliated? What is the character of the subepithelial tissue? Note the delicate nature of the fibers which form this stroma; the small, longitudinally directed vessels in this layer; the three or four broad folds into which the mucosa is raised. Observe the muscularis. Note that it consists of an inner circular and an outer longitudinal layer of smooth muscle fibers. Which layer is the more strongly developed? Examine the external layer of loosely arranged fibroelastic tissue, which contains the blood vessels and nerves passing to the wall of the oviduct. Note that this tissue, which forms the external coat of the oviduct, blends with that of the broad ligament.

Draw: showing the appearance and histological structure of the isthmus.

THE AMPULLA. Examine a section through the ampulla. Compare the mucosa of this section with that of the section of the isthmus previously studied. Apart from the presence of cilia, is there any difference to be observed between the ciliated and nonciliated cells? List any differences or similarities in the epithelial cells in these two sections. Observe the manner in which the mucosa is raised into a series of folds: note the complicated arrangement of the folds. Examine the muscularis, noting that it is considerably thinner in the ampulla than in the isthmus. Which of the two layers of the muscularis is the more changed? Observe the serosa, which consists of loosely arranged connective tissue. Identify the layer of mesothelial cells which lies upon the surface of the connective tissue. The mesothelial layer and the underlying connective tissue form a continuation of the peritoneal membrane which lines the abdominal cavity.

Draw: showing the structure of the ampulla as seen in the section.

Look for a series of small tubules in the connective tissue about the oviduct. These tubules are a part of the epoöphoron or parovarius, and are seen to consist of a low columnar or cuboidal epithelium resting on a dense layer of connective tissue in which a few scattered bundles of smooth muscle fibers may be observed. What do these tubules represent?

Draw a few of the tubules showing their histological structure and indicate their location in relation to the oviduct.

THE UTERUS

THE BODY OF THE UTERUS. Examine a section through the wall of the body of the uterus with the low power. Observe the mucosa (endometrium). Note its thickness (1–3 mm.). Examine its structure. Note that it consists of an epithelium resting on a stroma of reticular tissue. Observe the branched tubular glands (uterine glands) extending the entire depth of the stroma. Examine the muscularis (myometrium). Note that it consists of four poorly defined layers of smooth muscle fibers; an inner stratum submucosum in which the fibers are mainly longitudinal in direction with an intermingling of circular and oblique fibers; a stratum vasculare, the fibers of which are predominantly circular in direction. Note the numerous thin-walled blood spaces in this layer from which it receives its name; a stratum supravasculare, formed by an interweaving of circular and longitudinal fibers, the circular fibers being more numerous toward the stratum vasculare, the longitudinal fibers being more abundant in the external portion of the layer; a stratum subserosa, a thin external layer of longitudinally directed fibers.

It should be noted that, while this subdivision of the muscularis may have some value for descriptive purposes, it may be reduced to an inner layer of longitudinal fibers, a middle layer of circular fibers and an outer longitudinal layer.

Examine the serosa (perimetrium), a layer of thin, flattened mesothelial cells supported by a layer of loosely interwoven fibrous tissue. Note that this layer is an extension of the peritoneum of the abdominal cavity over the surface of the uterus.

Draw: showing the general structure of the uterus as seen with the low power.

Examine the section with high power. What type of epithelial cells line the uterine cavity? Note that while cilia are not constantly present, they are to be found on the free surfaces of some of the cells. Can you identify a basement membrane? Observe the branched tubular uterine glands. What is the extent of the uterine glands in the mucosa? What type of epithelium lines the glands? Compare the glandular epithelium with the epithelium of the uterine mucosa. Do any of the cells of the glandular epithelium bear cilia? Examine the stroma. Note its close resemblance to embryonic connective tissue. Observe, as well as the staining of the section permits, the branching processes of the connective tissue cells of the stroma. Do these processes anastomose with one another? What cells, previously studied, do the cells of the stroma suggest? Note that lymphocytes and granulocytes are present in the tissue spaces of the stroma. Observe the muscularis (myometrium). Note the unusual length of the slender, spindle-shaped smooth muscle fibers.

In the virgin uterus the muscle fibers are from 40–60 microns in length. In the gravid uterus the amount of muscular tissue is greatly increased, and there has been a growth of the individual fibers, which may measure from 300–500 microns in length.

THE CERVIX OF THE UTERUS. Examine a section through the cervix and adjacent portions of the vagina, using the low and then the high power. Observe the mucosa. Note its thickness; the tall folds (plicae palmatae) into which it is raised; the epithelium, consisting of tall columnar cells; the epithelial pits, which are depressions of the epithelium that appear to have a glandular character. These pits with their saccular outpocketings are to be seen between the folds. Observe the branched cervical glands. Note that the epithelium lining the cervical canal continues into both the pits and the glands and forms the epithelial lining. The cells which line the saccular outpocketings of these pits and the deep portions of the cervical glands secrete a mucoid substance. This substance forms a plug which closes the cervical canal during pregnancy. The secretion occasionally fills the sacculations, or glands, causing them to expand and form retention cysts (ovules of Naboth). Examine the muscularis. Note that the muscle fibers are arranged in inner longitudinal, middle circular, and outer longitudinal layers; the arrangement of the muscular layers being somewhat similar to that of the body of the uterus. However, the layers are more clearly defined in the cervix. If the section is through the lower end of the cervix it will include a portion of the wall of the vagina. Note the stratified squamous epithelium on the vaginal wall of the cervix; also on the opposing wall of the vagina. The space between these opposed surfaces represents the cavity of the vagina. In sections through the lower end of the cervix, the cervical canal may be lined by a stratified squamous epithelium.

THE MENSTRUATING UTERUS. Using the low and then the high power, examine sections through the wall of uteri representing various phases of the menstrual cycle. If possible these sections should show: the period of repair; proliferation; secretory period; and menstruation. Compare the various layers in these four sections and make a chart to record your findings.

Observe the mucosa. During what stage is the mucosa the highest? When is it the lowest? What changes take place in the appearance of the epithelium during these stages? When is the epithelium denuded? At what stage is it first apparent that regeneration of the epithelium is occurring? Examine the stroma. Note the changes which occur in the density of this tissue and at what stages these changes occur. Note the increase in the size and length of the uterine glands. During what stage are the glands most tortuous? How is this increase in the amount of glandular tissue in the stroma to be explained? Observe the changes which occur in the blood vessels of the mucosa during these various stages. Is there any indication that ischemia occurs during any of these stages? How do you account for such an occurrence? When is hemorrhage into the stroma first evident. Do the vascular changes occur uniformly in all vessels throughout the entire thickness of the stroma? Explain. Do the changes occurring during menstruation involve more than the mucosal layer?

THE PLACENTA

Examine a section of the placenta with the low power. Observe the amniotic membrane, consisting of a single layer of cuboidal cells—the amniotic ectoderm. Note that these cells rest on a layer of embryonic connective tissue. Identify the layer of embryonic connective tissue which is applied to the wall of the chorion. It is somewhat thicker than that on which the cells of the amnion rest. Observe the outer epithelium of the chorion, which consists of a single layer of cuboidal cells. This layer, which is frequently double, represents the chorionic ectoderm or trophoderm (trophoblast). Areas of cell proliferation are to be seen along the line of the trophoderm; the larger masses of these cells are known as proliferation islands, the smaller masses as proliferation knots. Note the branched processes of the chorion (chorionic villi) that may be seen projecting into a large space, the maternal blood space, between the chorion and the decidua basalis. Note that while the terminal portion of a few of the villi appear to be firmly fixed in the tissue of the decidua (anchored villi), the majority of the villi end in the blood spaces where they are surrounded by the maternal blood (floating villi).

With the high power, examine a villus which has been sectioned transversely. Observe the central area or core of embryonic connective tissue. Examine the epithelium by which the core is enclosed. Note that it consists of two rows of cells: an inner row of cuboidal cells (Langhan's layer) and an outer row of cells which present no definite boundaries (the syncytial layer). In examining sections of the placenta Langhan's layer may not be present as it tends to disappear in the later stages of pregnancy. Observe the blood vessels in the central core. Note their size and position. These vessels represent the terminal branches of the umbilical arteries and veins. Identify the proliferation islands and knots. Apply the same observations to a longitudinal section of a chorionic villus.

Examine the section of the placenta with the high power. Observe the densely compacted character of the stroma with which the chorionic structures are in contact (the compact layer of the decidua). Examine the decidual cells, to be identified by their size, the granular character of their cytoplasm, and the one or two vesicular nuclei which they contain. Locate and examine the portion of the decidual layer (uterine placenta) near the muscularis, in which the slitlike extensions of the deep portions of the uterine glands can be seen (the spongy layer of the mucosa). Note that the glands have lost their epithelium, and that their long axes are parallel with the surface of the muscularis. Account for this direction of the glandular spaces. Note the numerous blood vessels in this portion of the tissue. Note, also, the reduction of the muscularis to a relatively thin layer.

Draw: showing the histological structure of a chorionic villus; the appearance of the decidual cells.

Examine a section through the decidua vera with the low power. Observe that the decidual capsularis has disappeared, and that the chorion laeve rests directly on the decidua vera. Note that the epithelium of the chorion (trophoderm) which rests on the decidua, is composed of several layers of cells. Look for small areas of cell proliferation (proliferation islands and proliferation knots). These cell accumulations may be regarded as representing villi which are no longer being developed from the chorion laeva. Identify the amnion, consisting of a single layer of cuboidal cells (amniotic ectoderm). The amniotic and chorionic epithelia are separated by a small amount of embryonic connective tissue; the cleft between the tissue of the amnion and that of the chorion representing the extraembryonic coelomic cavity. The superficial portion of the decidua forms the compact layer; the deep portion forms the spongy layer, as in the decidua basalis. It is in the plane of this layer that the placenta is split off from the uterine wall.

Draw: showing the structural appearance of the decidua vera as seen in the section.

THE VAGINA AND THE FEMALE URETHRA

THE VAGINA

Hold a transverse section of a vagina (of a young subject) to the light and examine with a hand magnifier. What is the shape of the vaginal canal? Identify the urethra. What is its shape? What is its position in reference to the vaginal canal? Observe the wall of the vagina. Note the thickness of the epithelial layer. Compare it with the thickness of the subepithelial and muscular layers. Identify an external layer of fibrous tissue by which the vagina is attached to adjacent structures. Identify the urethrovaginal septum, which is a sheet of fibrous and muscular tissue that separates the vagina from the urethra.

Examine the section with the low power. What type of epithelium forms the lining of the vaginal canal? Note its unusual thickness, also that the thickness of the epithelium varies in different parts. How is this to be accounted for? Observe the subepithelial connective tissue. Note that the part that lies directly beneath the epithelium consists of a delicate reticular form of connective tissue in which lymphocytes, granulocytes and scattered small lymph nodules may be found. The connective tissue of the submucosa is relatively thick and consists of coarse bundles of collagenous and elastic fibers. Observe the muscularis. Note that it consists of a thick, inner circular layer and a thinner, outer longitudinal layer. Are these two layers of muscle distinct or is their arrangement more or less indefinite? Note the numerous vascular spaces between the muscle bundles which give the tissue a spongy appearance. Observe the ridges into which the mucosa is raised and which give the lumen its irregular outline. Note the highly developed connective tissue papillae which penetrate deeply into the epithelium. Is there any noticeable difference in the height of the papillae on the anterior and posterior wall? Observe the external covering of fibroelastic tissue by which the vagina is attached to adjacent structures. Is the fibrosa composed of compactly or loosely arranged fibers? Identify the numerous bundles of striated muscle fibers which form the sphincter vaginae muscle.

THE URETHRA

With the low power, examine the part of the section which includes the urethra. Observe the lumen of the urethra, noting its crescentic shape. What type of epithelium lines the urethra? Judging from the epithelium, at what level was the section cut? What changes occur in the epithelium lining the urethra in its course from the bladder to the external opening? Observe the subepithelial layer of fibroelastic tissue. Note the number of thin-walled venous spaces present. Identify the glandular structures which are similar to the glands of Littré in the male. Note the depressions in the epithelium (epithelial crypts) into which the glands open. Observe the bundles of smooth muscle fibers by which the subepithelial tissue is surrounded. What is the direction of the fibers in the two layers? In sections through the intermediate portion of the urethra, bundles of striated fibers which belong to the compressor urethrae muscle may be seen.

METHOD OF IDENTIFICATION AND DIFFERENTIATION OF BILE DUCT, URETER, VAS DEFERENS AND UTERINE TUBE

Bile duct, ureter, vas deferens and uterine tube are relatively small, epithelial lined, tubular structures which cause students some difficulty in identification.

Given an unknown slide for identification. Grossly the structure is seen to be a small, tubular structure, which may possibly be one of the above structures. Examine the tissue under low power. Locate and identify the epithelium lining the lumen. If the epithelium is a transitional epithelium the structure *must* be ureter.

If the epithelium is pseudostratified it is vas deferens. The vas also has a *very* strongly developed muscularis consisting of three layers of smooth muscle, an inner longitudinal layer which is quite thin, and a middle circular and outer longitudinal layer, both of which are relatively thick. In cross section there are four or five longitudinal folds which give the lumen a star-shaped appearance. In the ampulla of the vas, these folds become numerous and form crypts or recesses. This area is sometimes mistaken for the fimbriated extremity of the uterine tube since the epithelium may become a simple columnar in this region. The stroma of the fold in the ampulla of the vas, however, is more compact and less vascular than in the folds of the fimbriated end of the uterine tube.

If the epithelium is a simple columnar epithelium it may be bile duct or uterine tube. Look for ciliated cells. If cilia are present it is uterine tube. The stroma underlying the epithelium in the uterine tube is quite compact and contains many cells. The muscularis is well developed and in the isthmus consists of two layers, an inner circular and outer longitudinal. In the ampulla the outer longitudinal layer has thinned down to a few scattered muscle bundles, and in the fimbriated area only the inner circular layer is present. The mucosa of the uterine tube is thrown into a number of longitudinal folds which branch and anastomose. These folds are simpler and lower in the isthmus and increase in height and complexity as they reach the fimbriated end of the tube.

The characteristics which identify bile ducts are: simple columnar epithelium, and poorly developed muscularis, the layers of which are ill defined.

STUDY OF THE EYE

The Eyeball

Examine a section through the eyeball and lids, using the low power. Identify the conjunctiva. What type of epithelium forms the conjunctiva? Follow this epithelium as it passes upward on the ocular surface of the lid (palpebral conjunctiva) to the point where it arches across to the eyeball and becomes the bulbar conjunctiva. In following the course of the conjunctiva what change takes place in the type of epithelium as it reflects from the inner surface of the eyelid onto the sclera and cornea? Identify the space between the palpebral conjunctiva and the bulbar conjunctiva, which is known as the conjunctival sac. Identify the conjunctival fornix. Look for a few tubules belonging to the accessory lacrimal glands (Krause's glands) which may be seen near the fornix.

Observe the general form of the ocular bulb (eyeball) which is seen to consist of the segments of two circles. Observe the difference in the curvatures of the two segments. Identify the sclera and the cornea. Note that the sclera is continuous with the cornea at the sclerocorneal junction. Note the choroid which is a deeply pigmented layer lying close to the inner surface of the sclera. Follow the choroid anteriorly, noting that it forms a triangular thickening behind the sclerocorneal junction, the ciliary body. Follow the fold of the choroid which extends inward in front of the lens, forming the iris. Identify the pupillary border of the iris and the pupil. Examine the internal coat or retina of the posterior segment. Note where the optic nerve emerges from the eyeball. From this point trace the retina anteriorly. Note the abrupt change in thickness of this layer which occurs just behind the ciliary body. What causes this abrupt change in thickness. What is this zone called where the change occurs? Are there any visual elements (rods or cones) in the retina anterior to this zone? Follow the retinal layer forward on the inner surface of the ciliary body. As it continues over the ciliary processes it is known as the pars ciliaris, while the part which lies on the inner (posterior) surface of the iris, is called the pars iridica. Identify the lens and the suspensory ligament. Note the attachments of the suspensory ligament.

Identify the anterior and posterior chambers of the eye. What are the boundaries of each? What refractive media is found in these two chambers? What refractive media is found in the posterior segment of the eye? What is the difference in the consistency of these two media?

On the external surface of the posterior segment of the eye identify small bundles of striated muscle that are attached to the sclera. These are portions of the ocular muscles which bring about the voluntary movements of the eyeball. Try to identify Tenon's capsule and the space of Tenon.

In the section which has just been studied, or in one that has been prepared by special methods to bring out more clearly the details of the various structures, observe the structural details of the coats of the eye, first with low then with high power.

THE SCLERA. Identify the two layers of the sclera: the external layer or substantia propria, consisting of connective tissue fibers compactly woven into bundles which are arranged in lamellae. Note that the lamellae are alternately longitudinal and transverse in direction, the fibers which form the lamellae in one plane crossing at right angles those which form the lamellae of another plane. Minute interlamellar clefts or lymph spaces may be seen between the lamellae. Connective tissue cells (scleral corpuscles) containing melanin occupy these spaces. Observe the blood vessels which have penetrated the sclera on their way to the choroid; the internal layer or lamina fusca, consisting of a narrow strip of loosely interwoven connective tissue fibers, in which numerous chromatophores (pigmented connective tissue cells) are present.

THE CHOROID. The four layers usually described as belonging to the choroid are not easily distinguished in ordinary sections. They are as follows:

The *lamina suprachoroidea,* a thin layer of delicate, interlacing fibers among which are numerous pigmented cells. Observe the likeness of this layer to the lamina fusca of the sclera. Note the narrow cleft between the two layers, the suprachoroidal space, also the fibers which pass more or less obliquely from one layer to the other. What does this indicate regarding the relation of the two layers?

The *lamina vasculosa,* a relatively thick layer sometimes referred to as the "choroid proper." Note the large number of blood vessels it contains, the larger vessels, mostly venous, are toward the outer part of the layer, the smaller vessels being toward the inner part. Note the connective tissue between the vessels; also the pigmented connective tissue cells among the fiber bundles.

The *lamina choriocapillaris*, a relatively thin layer characterized by the number of capillary vessels it contains. Note the large caliber of these vessels.

The *lamina basalis,* a homogeneous layer which serves as a cuticular basement membrane for the pigmented cells of the retina and might be regarded as belonging more to the retina than to the choroid.

THE RETINA. Identify the layers of the retina as follows:

The *layer of pigmented cells,* consisting of a row of deeply pigmented cells which appear to be cuboidal as seen in vertical section.

Owing to the fact that the pigmented layer adheres more closely to the choroid than to the retina itself, it is likely to be separated from the layer of rods and cones in the section.

Note the delicate protoplasmic processes extending between the rods and cones from the inner surfaces of the pigmented cells.

The *layer of rods and cones,* the rods consist of a slender, elongated outer segment and a slightly thicker inner segment, the two segments being nearly equal in length. The cones consist of a short, narrow, outer segment and a thick, flask-shaped inner segment. Note that from three to five rods appear between each two cones.

The *external limiting membrane,* appearing as a thin, membranous structure between the layer of rods and cones and the outer nuclear layer. What type of tissue forms this layer?

The *external nuclear layer,* consisting of the cell bodies of the rods and cones containing the rod and cone nuclei. Note that the nuclei of the cone cells are larger than those of the rod cells and form a single row immediately internal to the outer limiting membrane. The rod cells are located at various levels and give considerable depth to the layer.

The *external reticular layer,* consisting of the processes of the rod and cone cells (the rod and cone fibers), and of the dendritic processes of the bipolar cells.

The *inner nuclear layer,* consisting of the nuclei of the bipolar, horizontal and amacrine cells.

The *inner reticular layer,* consisting of the axons of the bipolar cells and the dendritic processes of the ganglion cells.

The *ganglion cell layer,* a single row of large, multipolar ganglion cells. In certain areas the row of ganglion cells may appear double. In the macula lutea the number of ganglion cells is increased to several rows.

The *layer of nerve fibers,* the fibers of this layer are the axons of the ganglion cells. They are gathered in bundles on the inner surface of the retina. These bundles converge toward the optic disc, through which they pass to become the fibers of the optic nerve.

The *internal limiting membrane*, formed by the union of the expanded portions of the inner ends of Müller's fibers, constituting a thin membrane which intervenes between the nerve fiber layer and the vitreous body.

'Draw a portion of the section showing the structure of the coats of the eyeball as seen with the high power.

Examine, with the oil-immersion objective, a section of the retina prepared with Held's stain. Observe: the cells of the pigmented layer, noting their size; the form and position of their nuclei; the protoplasmic processes which extend from the inner surfaces of the cells between the rods and cones. Identify the rods and cones. Observe the rods. Note: their slender, outer segments; the transverse striation of these segments; the slightly enlarged inner segments; the vertically striated, dark body in the outer portion of this segment. Note that the rods are continued, internal to the outer limiting membrane, as a delicate protoplasmic thread, the rod fiber. The cell body is formed by an expansion of the protoplasm of the rod fiber in the outer nuclear layer, and contains the rod nucleus. Why do the rod nuclei occur at different levels in the outer nuclear layer? If possible, in the outer nuclear layer observe the manner in which a rod fiber ends in relation to a dendritic process of a bipolar cell. Observe the cones. Note: the relatively short, cone-shaped outer segment; the broad, flask shaped inner segment; the vertically striated, ellipsoidal body in the outer part of the thick segment; the protoplasmic body of the cone cell, just within the outer limiting membrane. Follow the broader, protoplasmic process of the cone cell into the outer reticular layer observing, if possible, the expanded foot plate in which it ends. Identify the bipolar cells, noting that they consist of deeply stained, slightly oval nuclei surrounded by a small amount of protoplasm. If the staining of the section permits, follow the processes of these cells. The dendrites extend into the outer reticular layer where they come into association with the end processes of the rod and cone fibers; the axons extend into the inner reticular layer in which they are associated with the dendrites of the ganglion cells. Identify both the horizontal and amacrine cells. In what way can these cells be distinguished from the bipolar cells, and from each other? Identify the ganglion cells, noting their stellate form; their dendritic processes, which extend (see above) into the inner reticular layer; their large, vesicular nuclei; their axons which continue as nerve fibers in the nerve-fiber layer. Observe the fibers of Müller; some of these fibers may be seen extending vertically through the section from the internal limiting membrane.

Draw: showing the histological structure of the retina as revealed by the section.

Construct a diagram on the basis of the above observations, showing the manner in which the various retinal elements are associated.

Examine a section through the macula lutea and the fovea centralis, using the high power. Observe the ganglion cell layer, noting the increase in the thickness of this layer due to the several rows of ganglion cells which it contains. Identify the inner nuclear layer. Compare the thickness of this layer in the macula with that of the inner nuclear layer in other parts of the retina. What is the difference? How is it to be accounted for? Examine the fovea centralis, a depression in the central part of the macula due to the thinning out of the layers of the retina. Note that the ganglion cell layer is absent from the fovea; that the inner and outer reticular layers merge into a single fibrous layer in which a few, scattered bipolar cells are present. Only cones are present in the fovea. Identify the fiber layer of Henle. This consists of the greatly lengthened cone fibers, which are directed obliquely from the fovea into the macula. In this case the cone cells with their contained nuclei do not lie immediately within the outer limiting membrane, but are at some distance from the cone segments.

Draw: showing the arrangements of the retinal elements in the macula lutea and fovea centralis.

ANTERIOR DIVISION OF THE EYE

Hold a section of the anterior division of the eye to the light and examine with a hand magnifier. Identify and note the relations of the following: the sclera; the cornea; the choroid; the ciliary body; the ciliary process; the lens; the iris; and, if the extent of the section permits, locate the ora serrata.

Using first the low and then the high power, observe the following:

THE SCLEROCORNEAL JUNCTION. Note that the fibers of the cornea are continuous with those of the sclera. Identify the bulbar conjunctiva, a layer of stratified squamous epithelium which is separated from the sclera by a thin substratum of fibrous tissue. Note that this subepithelial tissue disappears from beneath the epithelium as it extends over the cornea. The epithelial layer is slightly thinner over the cornea than over the sclera.

THE CORNEA. Examine the cornea and identify each of the five layers which compose it. Observe the epithelial layer (corneal conjunctiva), a thin layer of stratified squamous epithelium. What is the form of the basal layer of cells? Of the intermediate layers? Of the superficial layer? Identify the anterior basal membrane (Bowman's membrane), an apparently homogeneous structure lying immediately beneath the epithelial layer. Examine the substantia propria, which is the fibrous structure forming the principal portion of the cornea. Note the arrangement of the fibers in lamellae (corneal plates); the narrow lymph spaces between the plates (corneal spaces); the branched, stellate cells which occupy the corneal spaces (corneal corpuscles). If possible, identify the arcuate fibers, delicate fibers which pass from the lamellae in one level to those in another level. These fibers serve to bind the plates together.

THE CILIARY BODY. Locate the ciliary body and note that it is formed by the expansion of the anterior portion of the choroid. In conjunction with the ciliary body, examine the ciliary processes, which may be recognized as folds formed by an extension of the delicate, fibroelastic tissue of the ciliary body. Note, also, that the ciliary portion of the retina is continued over and between the folds. This portion of the retina consists of an outer, deeply pigmented layer and an inner layer of clear, epithelial cells. Identify the ciliary muscle. Note that it consists of bundles of smooth muscle fibers arranged in an outer layer of meridional fibers, originating from the sclera in the region of the sclerocorneal junction and, passing backward, are inserted into the anterior border of the orbicularis; a middle layer of radial fibers which curve downward toward the roots of the ciliary processes, into which they are inserted; an inner layer of circular fibers, forming a small bundle of smooth muscle fibers located at the inner angle of the ciliary muscle and cut transversely in the section. Note the position of these fibers close to the root of the iris.

THE IRIS. Observe the iris, which is a curtainlike fold which is attached peripherally to the ciliary body. Its free central portion extends inward in front of the lens. Note the space between the free central borders of the iris, the pupil; the portion of the iris adjacent to the pupil forms the pupillary border. Examine the structure of the iris. Note the stroma which consists of delicate collagenous fibers, with an intermingling of elastic fibers. Examine the numerous deeply pigmented, branched connective tissue cells (chromatophores) which may be observed in the stroma. Identify bundles of smooth muscle fibers forming a muscular ring about the pupillary border. These fibers belong to the sphincter pupillae muscle. Identify the spindle-shaped, contractile fibers (dilator pupillae muscle) located close to the pigmented epithelium. Observe the numerous blood vessels in the portion of the stroma toward the pigmented epithelium, the vascular layer. How far does this layer extend toward the pupillary border? Observe the thin layer of endothelial cells on the anterior surface. Examine the pigmented epithelium on the posterior surface of the iris that is the continuation of the nonvisual portion of the retina. It consists of a two-layered, epithelial structure which begins at the ora serrata and extends to the pupillary border of the iris. Where this layer covers the ciliary processes, note that the outer cells of the two cell layered structure is pigmented. This single layer of pigmented cells extends as far as the root of the iris, at which point both layers become pigmented. Note the abrupt manner in which this epithelium ends on the pupillary border.

The layer of retinal epithelium on the posterior surface of the iris consists of two rows of cells. This is not clearly evident when ordinary preparations are examined with the microscope, owing to the fact that both layers are deeply pigmented. When the tissue is bleached by special methods, the presence of the two layers of cells is readily demonstrated.

Again carefully examine the stroma and note that it can be divided into an anterior and posterior portion. The anterior portion is composed of branched, pigmented cells, supported by a relatively small number of connective tissue fibers—the anterior border layer. The posterior division of the stroma consists of collagenous and elastic fibers, and contains a relatively small number of chromatophores. This portion of the stroma, however, is plentifully supplied with blood vessels—the vascular layer.

THE PECTINATE LIGAMENT. Identify the pectinate ligament. Locate the iridial angle which is formed between the iris and the cornea. Observe the fibers in the form of an irregular network which constitutes the wall of the anterior chamber at the iridial angle. Trace these fibers from Descemet's membrane to the root of the iris. They constitute the pectinate ligament. The spaces between the fibers of the ligament are the spaces of Fontana. Can the delicate endothelium which lines the spaces of Fontana be discerned? Identify the canal of Schlemm (sinus venosus sclerae). A venous channel which encircles the eye close to the border of the cornea. Note that its inner wall is formed by some of the fibers of the pectinate ligament. Two or more spaces representing branches of the canal of Schlemm may be observed.

THE LENS. Examine the lens. A transparent, biconvex structure, located behind the iris and giving support to its pupillary border. The lens, together with the cornea, the aqueous humor and the vitreous body, form the refracting mechanism (refractive media) of the eye. Observe the difference between the anterior and posterior curvatures of the lens. Which is the greater? Identify the anterior and posterior poles, the mid-points of the anterior and posterior surfaces of the lens and the equator, represented by the border of the lens where the two curvatures meet. Observe the capsule, a thin, homogeneous membrane by which the substance of the lens is enclosed. Observe the lenticular epithelium, a single layer of cuboidal cells on the anterior surface of the lens immediately beneath the capsule. Follow the cells of the epithelium toward the equator, observing the manner in which they elongate to become the lens fibers. Note that the fibers, which are located in the middle of the lens, have a disintegrated appearance. They form the hard mass, known as the lens nucleus. Examine the suspensory ligament. Observe the hyaloid membrane, forming a cuticular layer on the inner surface of the retinal epithelium; the thickening of the membrane as it lies on the inner surface of the orbicularis; the manner in which it breaks up into fibers as it passes over and between the ciliary processes; the extension of these fibers from the ciliary body to their attachment to the capsule of the lens. The fibers which pass from the ciliary body to the lens form the suspensory ligament. Identify the zone occupied by the ligament as it encircles the equator of the lens, known as the zonule of Zinn, and the triangular canal of Petit.

Make a careful study of the structures of the anterior division of the eye and draw them in detail in the outline previously made.

THE OPTIC NERVE

Using the low power examine a section of the optic nerve as it emerges from the eyeball. Observe the dural sheath, following its fibers to their intermingling with the fibers of the sclera. Examine the pial sheath; follow its fibers and note that they are continuous with the inner portion of the sclera. Identify the intervaginal space between the dural and pial sheaths. Locate the thin arachnoid membrane dividing the intervaginal space into subdural and subarachnoid spaces. Observe the fibers crossing these spaces from the dura to the arachnoid and from the arachnoid to the pia. Locate the optic disc, the area in which the converging retinal fibers bend outward to pass through the wall of the eyeball and become the optic nerve. Note that the fibers are slightly arched as they make the turn, resulting in the formation of the physiological depression in the middle of the optic disc. Identify the lamina cribrosa, the portion of the wall of the eyeball through which the fibers pass. Note the manner in which the connective tissue fibers of the sclera cross the fibers of the optic nerve at right angles, as the fibers of the nerve pass through the lamina cribrosa. Observe the position of the retinal vessels in the axis of the nerve.

Draw: showing the entire structure of the optic disc, the manner in which the nerve fibers pass through the lamina cribrosa, and the structure of the optic nerve as revealed by the section.

Examine a cross section of the optic nerve. With the low power, observe the manner in which the nerve fibers are collected into bundles or fasciculi; the interfascicular connective tissue by which the bundles are surrounded; the fibrous sheaths which form the external investment of the nerve. Note that the interfascicular tissue is continued, between the bundles of nerve fibers, from the pial sheath. Observe the position of the retinal vessels.

Examine a fasciculus with the high power. Observe the axis cylinders of the nerve fibers, recalling that the axis cylinders are the axons of the cells of the ganglion cell layer of the retina. Identify the myelin sheaths by which the axis cylinders of the nerve fibers are invested. Note that the fibers of the optic nerve are not supplied with neurilemmal sheaths. Can neuroglial elements be identified among the nerve fibers? Observe the interfascicular connective tissue. In what respect does the optic nerve resemble a nerve trunk (such as the sciatic nerve)? In what way does it differ?

Draw: showing the structure of a fasciculus as it is seen with the high power.

THE EYELID

Hold a vertical section of the eyelid to the light and examine with a hand magnifier. Observe the form of the eyelid as seen in the section. Identify the cutaneous surface; the ocular (conjunctival) surface; the free (palpebral) border. Locate the bundles of striated muscle fibers belonging to the orbicularis palpebrarum muscle. Examine the connective tissue which lies beneath the epithelium covering the two surfaces and gives them their support; the tarsal plate (tarsus), located immediately in front of the epithelium of the ocular surface of the lid. Identify the Meibomian glands, noting their position in the tarsal plate. Observe the cilia (eyelashes) on the palpebral border of the lid.

Make an outline drawing of the eyelid, including the structures observed in the above study. The diagram should be sufficiently large to include the details to be observed in further studies of the section.

Examine the section with the low power; the observation of certain structural details, however, may require the use of the high power. Observe the epidermis; is it a relatively thick or thin layer? Examine the corium, the layer of dense, fibroelastic tissue which lies immediately beneath the epidermis. Note that the connective tissue between the corium and the orbicularis muscle is more loosely arranged. The epidermis and corium form the integument. The following structures should be observed in connection with the integument: the hair follicles, noting the delicate nature of the hairs; the sebaceous glands and their association with the hair follicles; the sweat glands, with their coiled, secreting portions lying deeply embedded in the corium. Wherever possible trace the ducts of these glands as they pass between the hair follicles to the surface of the skin. Note the increase in the thickness of the stratified squamous epithelium as it passes from the cutaneous surface to the palpebral border. Follow the continuation of the epithelium from the palpebral border to the conjunctival surface. How far does the stratified squamous epithelium extend upward on this surface? Note the point where it changes to a two or three layered columnar epithelium, the characteristic epithelium of the palpebral conjunctiva.

Goblet cells are present in considerable numbers in the conjunctival epithelium. These cells are peculiar in that they contain a mucoid substance, but do not appear to open on the surface of the epithelium. They are known as the mucous cells of Leydig.

Locate the bundles of transversely sectioned, striated muscle fibers occupying a considerable portion of the section between the cutaneous and conjunctival surfaces. These fiber bundles belong to the orbicularis palpebrarum. Note the mass of loosely arranged connective tissue fibers, the palpebral fascia, occupying the space between the orbicularis muscle and the conjunctival epithelium. Locate a thick platelike structure, consisting of densely compacted connective tissue, the tarsal plate located in the palpebral fascia immediately in front of the conjunctival epithelium.

The connective tissue fibers which form the tarsal plate are so densely compacted that, when taken between the fingers, the plate has the feel of cartilage. Because of its firmness and its position in the posterior wall, it not only supports the eyelid, but maintains as well a smooth surface which facilitates the movement of the lid over the eyeball.

Observe the large compound saccular glands located in the tarsal plate, the Meibomian glands. Note the similarity of these glands to the sebaceous glands already studied, the large, vertical duct lined with stratified squamous epithelium; the short necklike ducts by which the secreting bodies of these glands are attached to the common duct. Identify large stiff hairs, the cilia, of which there may be two or three rows on the palpebral border near its anterior angle. Note the large follicles for the cilia, deeply embedded in the corium; their oblique direction. Locate a small, isolated bundle of striated muscle fibers between the bases of the cilia and the inferior border of the tarsal plate; the ciliary muscle of Riolan. Observe: the small ciliary glands, which lie in relation to the ciliary follicles; large, coiled tubular sweat glands, the glands of Moll; modified sebaceous glands, the glands of Zeiss. Both the glands of Moll and Zeiss open either into the ciliary follicles or on the palpebral border. Identify a number of striated muscle fibers extending into the lid posterior to the orbicularis muscle, the levator palpebrae muscle. Note the manner in which these bundles end in tendinous fibers which spread out fanwise, some to be attached to the deep surfaces of the tarsal plate, others passing between the fiber bundles of the orbicularis muscle to end in the fascial tissue beneath the skin. Locate a small group of smooth muscle fibers, the superior tarsal muscle of Muller, which pass downward to attach to the upper border of the tarsal plate. Observe a small group of branched, tubular glands located in the loose connective tissue behind and above the upper border of the tarsal plate. Note the coarse, acidophilic granules contained in these glands, called the glands of Henle. If the section includes a part of the fornix, a number of small, serous glands, the accessory lacrimal glands (glands of Krause) may be seen in its supporting tissue.

Add the details observed in this study to the outline drawing of the lid previously made.

THE LACRIMAL GLANDS

Examine a section of the lacrimal gland with the low power. Observe that the groups of secreting tubules are separated by relatively broad septa of connective tissue. The portion of the glandular tissue between two broad septa is the equivalent of an individual gland. Note that the glandular elements are divided into smaller groups, the lobules, by narrower septa (interlobular septa) and the ducts located in these septa are the interlobular ducts. What type of epithelium lines these ducts? Observe the secreting tubules (alveoli; acini); the small ducts, the intralobular, or intercalary ducts, appearing in the section between the secreting tubules. Note that these ducts are lined with a cuboidal or low columnar epithelium.

Draw: showing the structural appearance of the gland as seen with the low power.

Examine the section with the high power. Observe the secreting tubules, noting that they are of two kinds: those in which the epithelium is composed of tall, columnar cells having a faintly granular cytoplasm and bordering a small lumen; those in which the epithelium consists of low columnar (or cuboidal) cells which have a densely granular cytoplasm and a large lumen.

The lacrimal glands are variously described as tubuloalveolar (tubuloacinar) and compound tubular glands. It is probable that the majority of sections studied will support the latter classification.

Small cells (basket cells; basal cells of most authors) are to be seen between the epithelial cells and the basement membrane. These cells are regarded as myoepithelial elements. Observe the interstitial connective tissue, in which may be seen numerous capillary branches, forming a network about the secreting tubules. Examine the intralobular (intercalary) ducts, surrounded by the secreting tubules. Note that these ducts possess a large lumen enclosed by a cuboidal epithelium. Observe the interlobular ducts, located in the interlobular septa. Wherever possible trace the connections from an interlobular duct through an intercalary duct to a secreting tubule.

Draw: showing in detail the histological structure of a lacrimal gland.

STUDY OF THE EAR

The External Ear

Examine a section through the auricle, using the low power. Observe: the irregularly curved plate of elastic cartilage which forms the principal support of the auricle; the perichondrial layer on either side of the cartilaginous plate; the skin, forming the outer covering of the ear. Note that here as elsewhere it consists of an epithelial layer, the epidermis, and a subepithelial layer, the corium, which together form an exceedingly thin layer over the auricle. Identify the hair follicles and sebaceous glands associated with the skin. Observe the subcutaneous connective tissue lying between the corium and the perichondrium on the posterior surface. Is there a similar layer on the anterior surface? Observe that a few sweat glands are present in the corium on the posterior surface.

The cellular character of the cartilage is discussed on p. 66. The elastic fibers and their distribution in the cartilage and surrounding tissues can best be observed in sections that have been prepared by using an elastic tissue stain.

Examine a longitudinal section of the external auditory meatus with the low power. Observe the cartilage ring that supports the outer third of the meatus. What kind of cartilage forms this ring? What type of tissue forms the support for the inner two-thirds? Observe the skin forming the lining of the canal. Note that a layer of subcutaneous connective tissue is interposed between the corium of the skin and the perichondrial layer of the cartilage. A similar layer may be observed between the skin and the periosteum in the roof of the bony portion of the meatus. Are there hair follicles in the skin of the canal? What is the extent of their distribution? Observe the small sebaceous glands associated with the follicles. Identify the ceruminous glands that are mingled with the other structures of the skin. They are coiled tubular glands resembling sweat glands. Note the extent of their distribution in the tissues which form the lining of the auditory canal. Identify the thin, membranous partition, the tympanic membrane, which forms the inner boundary of the external meatus. What is the position and direction of the tympanic membrane? Note that the epidermal layer increases in thickness and becomes deeply papillated just before it turns to pass onto the external surface of the tympanic membrane.

The Middle Ear

THE TYMPANIC MEMBRANE. Examine a section through the tympanic membrane, including a portion of the bone by which it is supported. Sections which include the greater part of the external auditory meatus should show the tympanic membrane as the internal boundary of the auditory canal.

Using the low power observe the general form and relations of the tympanic membrane: its direction, noting its slope from above downward; the slight inward bending, or concavity, of its outer surface; the tympanic sulcus or groove in the surrounding bone, into which the thickened peripheral border or annulus fibrosus is set; the malleus, a portion of which may be attached to the inner surface of the membrane. Note that the portion of the membrane above the attachment of the manubrium of the malleus is somewhat slack. This forms Shrapnell's membrane or the pars flaccida. The tightly drawn portion of the membrane below the attachment of the malleus is the pars tensa.

Draw: showing the appearance and relations of the tympanic membrane as seen in section.

Examine the tympanic membrane with the high power. Observe: its external covering of stratified squamous epithelium, noting that it is continuous with and much thinner than the epithelium which forms the lining of the external auditory meatus; the fibrous portion (substantia propria) of the membrane. Distinguish between the radial fibers which form the outer layer and the concentrically arranged circular fibers which form the inner layer; the mucous layer, covering the inner surface of the membrane, noting that both the layer of flattened epithelial cells, and the tunica propria on which it rests, are continuous with the mucous membrane that forms the lining of the tympanic cavity. If the malleus is represented in the section, note that it is covered by an extension of the mucous membrane; identify the annulus fibrosus, a thickened ring of fibrous tissue which forms the periphery of the tympanic membrane, noting that it is set in a deep groove, the sulcus tympanicus, in the bony ring supporting the tympanic membrane. Observe the manner in which the fibers of the annulus fibrosus converge as they enter the tympanic membrane to form its outer or radial fiber layer.

Draw: showing the histological structure of the tympanic membrane, as seen with the high power.

THE EUSTACHIAN TUBE

Examine a transverse section of the cartilaginous portion of the Eustachian tube with the low power. Observe: the cartilaginous plate (the side on which it lies is to be regarded as the inner side of the tube). Note how the cartilage forms a groove in which the tube rests, by bending around its outer end. What type of epithelium lines this portion of the tube? Note the numerous small depressions in the epithelium which are lined by mucus-secreting cells. Observe the thick layer of fibroelastic tissue surrounding the epithelium and completing the wall of the tube; the mucous glands in the subepithelial connective tissue; bundles of striated muscle fibers. Those belonging to the tensor palati muscle are cut more or less longitudinally and lie on the outer side, while the fibers of the levator palati muscle are sectioned transversely and lie below and a little to the inner side of the tube. In sections through the "aditus," or opening of the tube into the nasopharynx, note that the connective tissue by which it is surrounded is filled with lymphoid tissue mainly in the form of nodules. These masses of lymphoid tissue are known as the tubal tonsils.

Although called tubal tonsils, because of their relation to the Eustachian tube, strictly speaking these masses of lymphoid tissue belong to the lymphoid tissue in the roof of the pharynx, known as the pharyngeal tonsils.

Draw: showing the histological structure of the Eustachian tube as seen in the section.

THE INTERNAL EAR

Hold a section of the semicircular canal to the light and examine with a hand magnifier. Identify the membranous and bony portions of the semicircular canals.

Examine the section with the low power where it passes through a semicircular canal. What is the relation of the membranous to the bony canal? Identify the perilymph space, noting that it includes the greater part of the bony canal. Where is the endolymph space? What is the shape of the semicircular canal? Note that its outer layer is adjacent to and merges with the periosteal layer of the bone. Identify the fibrous trabeculae that pass from the periosteal tissue of the bony canal to the wall of the membranous canal.

Examine the membranous canal with the high power. Observe that the epithelial lining of the canal consists of flattened, squamous cells. A narrow strip of thickened epithelium, the raphe, may be seen on the convex side of the canal. What does this signify? Note the densely compacted connective tissue which forms the outer wall of the membranous canal. Observe the minute serrations, formed by papillalike elevations of the subepithelial tissue. Note the manner in which the epithelium passes over these elevations. Observe the periosteal lining of the bony canal, noting the delicate connective tissue fibers of which it is composed. Follow the trabeculae or fibrous strands in which this tissue is continued from the inner surface of the wall of the bony canal to the outer, fibrous layer of the membranous canal. Identify the layer of mesothelial cells lying on the periosteal layer and forming the immediate lining of the perilymph space. Note that the tissue, formed by these cells, invests the trabeculae and is continued over the fibrous layer of the membranous canal.

Note, where the utricle and saccule can be seen in the section, that the structure of their membranous walls is similar to that of the membranous semicircular canals.

THE MACULA. Examine with the high power a section of the macula in either the utricle or the saccule. Observe: the increase in thickness of the periosteal tissue in the region of the macula. Follow the cells of the epithelium, noting that the flattened cells become cuboidal as they approach the border of the macula, and low columnar as they pass over the border. There are two kinds of cells which form the epithelium on the surface of the macula: the sustentacular cells, which are tall columnar cells presenting broad, expanded basal portions which rest on a clearly defined basement membrane, and in which their nuclei are located, and narrow, distal portions extending to the surface of the epithelium; the sensory or hair cells. These cells are relatively broad, cylindrical elements, which extend about half way from *the surface of the epithelium to the basement membrane. Note that the* spherical nuclei of these cells are located in their rounded, basal portions, which have the appearance of resting on the "shoulders" of the sustentacular cells. The surfaces of both the sustentacular and hair cells are provided with cuticular plates which interlock and form a continuous membrane over the surface of the macula. Observe the stiff, hair-like processes which project from the free surfaces of the hair cells, each of which gives rise to a single process. Examine the otolithic membrane, a gelatinous, platelike structure separated from the epithelium of the macula by a narrow, endolymph space. Note that the processes of the hair cells cross this space and are embedded in the otolithic membrane.

The otoliths or otoconia are minute particles of calcium carbonate which have crystallized about an organic nucleus. They are present in the otolithic membrane in the living condition, but can be demonstrated only in specially prepared material.

Identify the well-developed basement membrane on which the cells of the epithelium rest, and observe the thickened subepithelial layer of connective tissue. The thickness of this layer is due, not only to an increase in the number of connective tissue fibers, but also to the nerve fibers passing through it to the sensory cells.

THE CRISTA. Using the high power examine a section through the ampulla of a semicircular canal which includes a crista. Observe the form of the crista, noting that it is taller and narrower than the macula which is relatively low and broad. The form of the crista is determined by the manner in which the subepithelial connective tissue, which is a modification of the periosteal layer, is raised into a moundlike ridge. Examine the epithelium which covers the supporting fibrous tissue, noting that it consists of sustentacular and sensory (hair) cells, essentially similar to those observed in the macula. Identify the cupula, a dome-shaped gelatinous structure which lies above the summit of the crista, to which it bears the same relation that the otolithic membrane bears to the macula.

If sections through the temporal bone of one of the smaller animals are properly made the fibers of the vestibular division of the auditory nerve may be traced to the cells of the vestibular ganglion located in the internal auditory meatus, and from the cells of the ganglion through the canal in the bone to the subepithelial tissue, through which it passes to be distributed to the sensory cells of the macula and crista. In these sections it will be noted that the fibers which pass to the macula and crista belong to the same branch. In tracing these fibers from the macula and crista to the vestibula ganglion and noting the relation of the ganglion cells to the vestibular branch of the auditory nerve, it should be borne in mind that, although they cannot be followed in the same manner in sections of the human ear, the relations are essentially the same in all of the higher animals, man included.

THE COCHLEA. Examine a section of the cochlea with a hand magnifier. Observe the segments of the cochlear canal as it winds around the central pillar or modiolus. Note the manner in which the modiolus tapers from base to apex. Identify the bony spiral lamina, a shelflike process extending from the modiolus into the cochlear canal.

Observe the basilar membrane (membranous spiral lamina). Note that it extends from the outer border of the bony lamina to the lateral wall of the cochlear canal, completing the partition between the upper and lower chambers of the canal.

Note the division of the chamber above the partition into two parts by a thin membrane (membrane of Reissner), which extends from the outer wall of the canal obliquely downward and inward. The cochlear canal is divided, in this manner, into three compartments: an upper compartment, above Reissner's membrane—the scala vestibuli; a lower compartment, below the partition formed by the spiral lamina and the basilar membrane—the scala tympani; and an intermediate compartment between Reissner's membrane and the basal membrane—the scala intermedia or cochlear duct.

Note that this division is repeated in each segment; bearing in mind that the segments are parts of a continuous canal which winds about the modiolus, and that the structures noted in the above study follow the spiral turns of the cochlea.

Draw, showing the arrangement of the segments of the cochlea and their relation to the modiolus as seen in the section; the division of the cochlear canal into scala vestibuli, scala tympani and cochlear duct.

Examine a single segment of the cochlear canal with the low power. Observe the position and form of the modiolus: the external wall of the segment; the bony spiral lamina extending shelflike from the modiolus toward the outer wall; the spiral ligament, a crescent-shaped thickening of the periosteal tissue of the lateral wall. Note that the spiral ligament begins in the scala vestibuli, forms the lateral wall of the cochlear duct, in which it attains its highest development, and ends below the level of the basilar membrane in the scala tympani. It is thus seen that the spiral ligament forms an important part of the lateral wall of the three divisions of the cochlear canal. Identify the crista basilaris, a projection of the spiral ligament, to the apex of which the outer part of the basilar membrane is attached. Locate the basilar membrane, extending outward from the bony spiral lamina, to which its inner portion is attached, to the apex of the crista basilaris; Reissner's membrane, a thin, membranous structure extending from near the upper border of the spiral ligament, downward and inward to a point near the base of the bony spiral lamina. Note that Reissner's membrane forms the "roof" of the cochlear duct and separates it from the scala vestibuli. Identify: the spiral prominence, a rounded elevation of the spiral ligament, a short distance above the crista basilaris; the external spiral sulcus, a shallow groove between the spiral prominence and the crista basilaris. Examine the fibrous tissue of the spiral ligament above the spiral prominence, noting that it is covered by a pseudostratified or stratified columnar epithelium; also that the loose tissue beneath the epithelium is filled with blood vessels, forming the stria vascularis. Note the extent of the spiral ligament above Reissner's membrane and below the apex of the crista basilaris. Identify: the organ of Corti, a highly specialized, epithelial structure resting on the basilar membrane; the fibers of the cochlear division of the auditory nerve. Trace the main branch of the nerve as it passes in the central canal from the base of the modiolus to its apex. Follow the branches passing laterally from the fibers in the central canal to the cells of the spiral ganglion which are located in the spiral canal at the base of the bony spiral lamina. Follow the fibers from the cells of the spiral ganglion as far as possible towards the organ of Corti.

With the high power examine the organ of Corti, using the same section or one that has been prepared especially for this study. The best observations are made with the oil-immersion objective. Observe the limbus spirale, noting its position on the medial side of the cochlear duct. It is seen to consist of an upper portion, formed by a thickening of the periosteal tissue at the base of the bony spiral lamina—the vestibular lip (labium vestibulare); and a lower portion—the tympanic lip (labium tympanicum). The tympanic lip should be followed outward to a point near the lateral border of the bony spiral lamina. Locate the well-defined groove between the vestibular and tympanic lips, the internal spiral sulcus. The upper surface of the vestibular lip is covered by a layer of flattened epithelial cells. Follow these cells and note that they become cuboidal as they pass over the border of the lip and form the lining of the internal sulcus. The cells are flattened as they continue outward on the tympanic lip of the limbus. At the border of the tympanic lip locate the inner sustentacular or border cells. What is the shape of these cells? Observe the single row of inner hair cells. Observe the shape of the inner hair cells; note that they extend only part way through the depth of the epithelium and are supported in part by the border cells. Identify the inner phalangeal cells, which appear as slender, cellular elements that lie between the inner hair cells and the inner pillars of Corti. In well-prepared material it will be possible to observe that the surfaces of the border cells, the hair cells and the inner phalangeal cells are provided with cuticular plates. These plates interarticulate and provide a support for the hair cells. Examine the hairlike processes of the hair cells, which project through the cuticular plates into the cochlear duct. Observe the pillars of Corti, of which there are two sets, the inner and the outer pillars. Each pillar is seen to consist of an expanded head, appearing somewhat triangular in section, a narrow body by which the head is supported, and the foot by which it is attached to the basilar membrane. Note: the manner in which the heads of the outer pillars are articulated with the heads of the inner pillars; that the rodlike bodies of the pillars diverge as they pass toward the basilar membrane, forming a triangular space between them, the tunnel of Corti; the mass of protoplasm containing a large nucleus, the pillar cells, at the foot of each pillar on the tunnel side. Identify the cells of Deiters (outer phalangeal cells). Three or four rows of tall, columnar cells external to the outer pillars of Corti. Note that the proximal portions of these cells in which their nuclei are located are considerably broader than their distal portions, which form narrow phalangeal processes. Each phalangeal process is expended at the surface of the epithelium and bears a cuticular plate. In properly stained material a small, rodlike bundle of tonofibrils can be demonstrated in these cells.

The relation between the pillar cells and the cells of Deiters is readily apparent: the pillar cells being a modified form of Deiters' cells.

Observe the outer hair cells. How many rows of these can be observed in the section? Note the position of the hair cells between the phalangeal process of the cells of Deiters. How does their form compare with that of the inner hair cells? How far do they extend toward the basilar membrane? The outer hair cells, like the hair cells, are provided with cuticular plates through which the hairlike processes of the cells project. Examine the cells of Hensen which form three or more rows of tall, columnar cells external to the cells of Deiters. Note their slender, proximal portions which rest on the basilar membrane, and their expanded distal portions in which their spherical nuclei are located. Follow the cells of Hensen, noting that they become progressively lower until they merge with the layer of cuboidal cells, known as the cells of Claudius. The cells of Claudius can be identified by their cuboidal form, and the fact that they form the epithelium of the outer portion of the basilar membrane. Note that they are continued as the epithelial lining of the external spiral sulcus. Observe that the cells of Claudius differ from the other cells of the organ of Corti by their small nuclei and clear, nongranular cytoplasm. Examine the basilar membrane on which the organ of Corti rests. Note that its inner attachment is to the free border of the bony spiral lamina on which it lies, and that it joins the crista basilaris laterally. Its fibers can be seen in the crista, where they have the appearance of converging toward the membrane. They should be interpreted, however, as fibers from the basilar membrane which are being dispersed in the spiral ligament. On the tympanic side of the basilar membrane is a layer of loosely arranged fibrous tissue, the tympanic covering layer. Identify the part of this layer which lies beneath the zona arcuata. Note the number of small blood vessels in this portion of the layer; also the larger vessel beneath the tunnel of Corti, the vas spirale, into which the smaller vessels empty. Identify the zona pectinata, noting that the tympanic covering layer beneath this portion of the membrane, is slightly thicker than that beneath the zona arcuata. Also note that it is not supplied with blood vessels.

The principal characteristic of the tympanic covering layer is the loose arrangement of its fibrous elements. Although it contains numerous, spindle-shaped connective tissue cells, its surface is not covered by a continuous layer of mesothelial cells.

Examine the vestibular covering layer, which is a more or less homogeneous layer on which the cells of the organ of Corti rest. A few fibers and some scattered nuclei may be observed in this layer. Locate the membrane of Reissner. Examined with the higher powers, the membrane of Reissner is seen to consist of a thin substantia propria which is covered externally by a layer of thin mesothelial cells continuous with the lining of the scala vestibuli, its inner (cochlear) surface being covered by a layer of flattened, ectodermal cells which are continuous with the epithelial lining of the cochlear duct. Observe the tectorial membrane. Note that it consists of numerous fibers which give it a striated appearance. The fibers are held together by a gelatinous, interfibrillar substance and extend in radial fashion from the border of the vestibular lip of the spiral limbus over the organ of Corti as far as the lateral row of the outer hair cells.

The tectorial membrane is formed by a fusion of the cuticular plates of the epithelium covering the upper surface of the vestibular lip of the limbus.

Trace the fibers of the cochlear division of the auditory nerve from the spiral ganglion to the organ of Corti. Note especially where the fibers pass through the tunnel of Corti and the space of Nuel.

Draw: showing in detail the structure of the organ of Corti.

References for Suggested Readings

The following list of references is designed for use as additional readings in connection with the subjects studied. The titles, which have been chosen from a voluminous literature, are fairly typical of the papers in which the results of the researches in histology have been reported.

Only those titles which are in English have been selected. The student who wishes to pursue his reading beyond the papers listed here should turn to the more complete bibliographies with which these papers are supplied and in which the more important titles in French and German will be found.

The use that is made of these references will be determined by the judgment of the instructor and the curiosity and interest of the student. Their purpose is to direct the student to those lines of reading which will lead to a familiarity with the investigations through which our knowledge of the facts of histology have been obtained.

1. REFERENCE TEXTS

Bremer, J. L., and H. L. Weatherford: "A Text-book of Histology," Philadelphia, *The Blakiston Company*, 1944.

Cowdry, E. V.: "A Textbook of Histology," Philadelphia, Lea and Febiger, 1944.

Maximow, A. A., and Wm. Bloom: "A Textbook of Histology," Philadelphia, W. B. Saunders Co., 1942.

Smith, P. E., and W. M. Copenhaver: "Bailey's Text-book of Histology," Baltimore, The *Williams and Wilkins* Company, 1941.

2. MICROSCOPICAL TECHNIQUE

Bensley, R. R., and S. H. Bensley: "Handbook of Histological and Cytological Technique," Chicago, University of Chicago Press, 1941.

Conn, H. J.: "Biological Stains: A handbook on the nature and uses of the dyes employed in the biological laboratory," 4th ed., Geneva, N. Y., Biotechnical Publication, 1940.

Lee, A. B.: "Bolles Lee's Microtomist's Vade-mecum," 9th ed., Philadelphia, The *Blakiston Company*, 1928.

Mallory, F. B., and J. H. Wright: "Pathological Technique," 8th ed., Philadelphia, W. B. Saunders Co., 1924.

McClung, C. E.: "Handbook of Microscopical Technique for Workers in Animal and Plant Tissues," New York, P. B. Hoeber, Inc., 1937.

3. THE MICROSCOPE

Gage, S. H.: "The Microscope," Ithaca, N. Y., Comstock Publishing Co., 1932.

4. THE CELL.

Beams, H. W., and R. L. King: The effects of ultracentrifuging upon the Golgi apparatus in the uterine gland cells, *Anat. Record*, 59: 363, 1934.

Beams, H. W., and H. W. Kirshenblit: Ultracentrifugation of rat spinal ganglion cells, with special reference to neurofibrillae, *Anat. Record*, 76: 95, 1940.

Bensley, R. R.: On the nature of the canalicular apparatus of animal cells, *Biol. Bull.*, 19: 179, 1910.

Bensley, R. R., and I. Gersh: Studies on cell structure by the freezing drying method. Part 1, *Anat. Record*, 57: 205; Part 2, 217; Part 3, 369; 1933.

Bensley, R. R., and N. L. Hoerr: Studies on cell structure by the freezing-drying method, Part 6. *Anat. Record*, 60: 449, 1934.

Bloom, W.: Cellular differentiation and tissue culture, *Physiol. Rev.*, 17: 589, 1937.

Carleton, A.: A rhythmical periodicity in the mitotic division of animal cells, *J. Anat.*, 68: 251, 1934.

Carrel, A.: Tissue culture and cell physiology, *Physiol. Rev.* 4: 1, 1924.

Chambers, R.: The physical structure of protoplasm as determined by microdissection and injection, Cowdry's "General Cytology," 235, 1924.

———: Recent developments of the micro-manipulative technique and its application, *J. Roy. Microscop. Soc.*, 60: 113, 1940.

Cowdry, E. V.: The mitochondrial constituents of protoplasm. Contrib. to Embryol., *Carnegie Inst. of Wash. Pub.*, No. 271: 39, 1918.

Gersh, I.: Recent developments in histochemistry, *Physiol. Rev.*, 21: 242, 1941.

Gray, James: "A Textbook of Experimental Cytology," Cambridge, Eng., The University Press, 1931.

Kirkman, H., and A. E. Severinghaus: A review of the Golgi apparatus, *Anat. Record*, 70: 413 and 557; 71: 79, 1938.

Kite, G. L.: The physical properties of protoplasm of certain animal and plant cells, *Am. J. Physiol.*, 33: 146, 1913.

Knisely, M. H.: A method of illuminating living structures for microscopic study, *Anat. Record*, 64: 499, 1936.

———: An improved fused quartz living tissue illuminator, *Anat. Record*, 71: 503, 1938.

Lewis, W. H., and M. R. Lewis: Behavior of cells in tissue cultures, in Cowdry's "General Cytology," Chicago, The Univ. of Chicago Press, 385, 1924.

McClung, C. E.: The chromosome theory of heredity, in Cowdry's "General Cytology," Chicago, The Univ. of Chicago Press, 609, 1924.

Scott, G. H.: A critical study and review of the method of microincineration, *Protoplasma*, 20: 133, 1933.

Scott, G. H., and D. M. Packer: The electron microscope as an analytical tool for the localization of minerals in biological tissues, *Anat. Record*, 74: 17, 1939.

Weiss, P., and H. Wang: Neurofibrils in living ganglion cells of the chick, cultivated in vitro, *Anat. Record*, 67: 105, 1936.

Wilson, E. B.: "The Cell in Development and Heredity," New York, The Macmillan Company, 1928.

5. EPITHELIUM

Arey, L. B.: Wound healing, *Physiol. Rev.*, 16: 327, 1936.

Chambers, R., and G. S. de Rényi: The structure of the cells in tissues as revealed in microdissection, *Am. J. Anat.*, 35: 385, 1925.

Lewis, F. T.: Mathematically precise features of epithelial mosaics: Observations on the endothelium of capillaries, *Anat. Record*, 55: 323, 1933.

Lucas, A. M.: Ciliated epithelium, in Cowdry's "Special Cytology," 2nd ed., 1: 407, 1932.

Macklin, C. C., and M. T. Macklin: The intestinal epithelium, in Cowdry's "Special Cytology," 2nd ed., 1: 233, 1932.

Proetz, A. W.: "Applied Physiology of the Nose," St. Louis, Mo., Annal Pub. Co., 1941. Cilia: Chapters 12, 181; 13, 192; 14, 222; 15, 239.

Wolbach, S. B., and P. R. Howe: Epithelial repair in recovery from vitamin A deficiency. An experimental study, *J. Exp. Med.*, 57: 511, 1933.

6. CONNECTIVE TISSUES

Bensley, S. H.: On the presence, properties and distribution of the intercellular ground substance of loose connective tissue, *Anat. Record*, 60: 93, 1934.

Carrel, A., and A. H. Ebeling: The fundamental properties of the fibroblast and the macrophage, *J. Exp. Med.*, 44: 261, 1926.

Clark, E. R., and E. L. Clark: Microscopic studies of the new formation of fat in living adult rabbits, *Am. J. Anat.*, 67: 255, 1940.

Dees-Mattingly, M.: On the nature and framework of the fat-corpuscle, *Anat. Record*, 36: 175, 1927.

Evans, H. M., and K. J. Scott: On the differential reaction to vital dyes exhibited by the two great groups of connective tissue cells, Contrib. to Embryol., *Carnegie Inst. of Wash. Pub.*, No. 47, 10: 1, 1921.

Foot, N. C.: Chemical contrasts between collagenous and reticular connective tissue, *Am. J. Path.*, 4: 525, 1928.

Isaacs, R.: The structure and mechanics of developing connective tissue, *Anat. Record*, 17: 243, 1919.

Lewis, M. R.: Development of connective tissue fibers in tissue cultures of chick embryos, Contrib. to Embryol., *Carnegie Inst. of Wash. Pub.* No. 17, 6: 45, 1917.

Lewis, W. H.: Is mesenchyme a syncytium? *Anat. Record*, 23: 177, 1922.

Mall, F. P.: Development of the connective tissues from the connective tissue syncytium, *Am. J. Anat.*, 1: 329, 1902.

Maximow, A.: Development of argyrophile and collagenous fibers in tissue cultures, *Proc. Soc. Exp. Biol. & Med.*, 25: 439, 1928.

CARTILAGE

Elliott, H. C.: Studies on articular cartilages, *Am. J. Anat.*, 58: 127, 1936.

Fell, H. B.: Chondrogenesis in cultures of endosteum, *Proc. Roy. Soc. (London)*, B, 112: 417, 1933.

Nunnemacher, R. F.: Experimental studies on the cartilage plates in the long bones of the rat, *Am. J. Anat.*, 65: 253, 1939.

BONE

Arey, L. B.: Origin, growth and fate of osteoclasts and their relation to bone absorption, *Am. J. Anat.*, 26: 315, 1920.

Bast, T. H., W. E. Sullivan, and F. D. Geist: The repair of bone, *Anat. Record*, 31: 255, 1925.

Clark, E. R., and E. L. Clark: Microscopic observations on new formation of cartilage and bone in the living mammal, *Am. J. Anat.*, 70: 167, 1942.

Dodds, G. S.: Osteoclasts and cartilage removal in endochondral ossification of certain mammals, *Am. J. Anat.*, 50: 97, 1932.

Fell, H. B.: The osteogenic capacity in vitro of periosteum and endosteum isolated from the limb skeleton of fowl embryos and young chicks, *J. Anat.*, 66: 157, 1932.

Huggins, C.: The composition of bone and the function of the bone cell, *Physiol. Rev.*, 17: 119, 1937.

McLean, F. C., and W. Bloom: Calcification and ossification. Calcification in normal growing bone, *Anat. Record*, 78: 333, 1940.

7. BLOOD AND BONE MARROW

Arey, L. B.: Normal shape of the mammalian red blood corpuscle, *Am. J. Anat.*, 22: 439, 1917.

Bloom, W.: Lymphocytes and monocytes: Theories of hematopoiesis, Handbook of Hematology (Downey, ed.), 1: 373, 1938.

Bunting, C. H.: The granular leucocytes, in Cowdry's "Special Cytology," 2: 683, 1932.

Cooke, W. E., and E. Ponder: "The Polynuclear Count," Philadelphia, J. B. Lippincott Company, 1927.

Danchakoff, V.: Origin of the blood cells, *Anat. Record*, 10: 397, 1916.

Doan, C. A.: Bone Marrow. Normal and pathologic physiology with special reference to diseases involving the cells of the blood, Handbook of Hematology (Downey, ed.), 3: 1839, 1938.

Downey, H.: The myeloblast—Its occurrence under normal and pathological conditions, and its relations to lymphocytes and other blood cells, *Folia Haematol.*, 34: 65, 145, 1927.

———: The myeloblast, Handbook of Hematology, (Downey, ed.), 3: 1963, 1938.

Fowler, W. M.: "Hematology for Students and Practitioners," New York, P. B. Hoeber, Inc., 1945.

Henderson, M.: A review of the motility of the leucocytes of the blood with a few additional observations, *Anat. Record*, 38: 71, 1928.

Howell, W. H.: The life-story of the formed elements of the blood, especially of the red corpuscles, *J. Morphol.*, 4: 57, 1890.

Jordan, H. E., and C. C. Speidel: The fate of the mammalian lymphocyte, *Anat. Record*, 26: 223, 1923.

Kolouch, F. Jr.: The lymphocyte in acute inflammation, *Am. J. Path.*, 15: 413, 1939.

Krumbhaar, E. B.: The erythrocyte, in Cowdry's "Special Cytology," 2: 553, 1932.

Maximow, A.: The lymphocytes and plasma cells, in Cowdry's "Special Cytology," 2: 601, 1932.

Minot, G. R.: Megacaryocytes in the peripheral circulation, *J. Exp. Med.*, 36: 1, 1922.

Rous, P.: Destruction of red corpuscles in health and disease, *Physiol. Rev.*, 3: 75, 1923.

Sabin, F. R.: Studies of living human blood cells, *Bull. Johns Hopkins Hosp.*, 34: 277, 1923.

———: Bone marrow, in Cowdry's "Special Cytology," 1: 505, 1932.

Sabin, F. R., and F. R. Miller: Normal bone marrow, Handbook of Hematology (Downey, ed.), 3: 1789, 1938.

8. MUSCULAR TISSUES

Carr, R. W.: Muscle-tendon attachment in the striated muscle of the fetal pig; demonstration of the sarcolemma by electric stimulation, *Am. J. Anat.*, 49: 1, 1931.

Cohn, A. E.: Cardiac muscle, in Cowdry's "Special Cytology," 2: 1127, 1932.

Eastlick, H. L.: A cytological study of the Golgi substance of striated muscle of vertebrates, *J. Morphol.*, 61: 399, 1937.

Fulton, J. F.: "Muscular Contraction and the Reflex Control of Movement," Baltimore, The Williams & Wilkins Company, 1926.

Gasser, H. S.: Contracture of skeletal muscle, *Physiol. Rev.*, 10: 35, 1930.

Hill, A. V.: The revolution in muscle physiology, *Physiol. Rev.*, 12: 56, 1932.

Hunter, J. I.: The sympathetic innervation of striated muscle, *Brit. Med. J.*, 1: 197, 1925.

Jordan, H. E.: Structural changes in striped muscle during contraction, *Physiol. Rev.*, 13: 301, 1933.

Jordan, H. E., and K. B. Steele: A comparative microscopic study of the intercalated discs of vertebrate heart muscle, *Am. J. Anat.*, 13: 151, 1912.

McGill, C. The structure of smooth muscle in the resting and in the contracted condition, *Am. J. Anat.*, 9: 493, 1909.

Meigs, E. B.: Striated and smooth muscle, in Cowdry's "Special Cytology," 2: 1089, 1932.

Sacks, J.: Changing concepts of the chemistry of muscular contraction, *Physiol. Rev.*, 21: 217, 1941.

Speidel, C. C.: Studies of living muscles. II. Histological changes in single fibers of striated muscle during contraction and clotting, *Am. J. Anat.*, 65: 471, 1939.

Tiegs, O. W.: Observations on the structure of striated muscle fibre, *Proc. Roy. Soc. (London)*, 116: 38, 1934.

9. NERVOUS TISSUES

Bardeen, C. R.: The growth and histogenesis of the cerebrospinal nerves in mammals, *Am. J. Anat.*, 2: 231, 1903.

Barker, L. F.: "The Nervous System and Its Constituent Neurons," New York, D. Appleton & Company, 1899.

Boeke, J.: Nerve endings, motor and sensory, "Cytology and Cellular Pathology of the Nervous System," (Penfield, Ed.), 1: 241, 1932.

Fulton, J. F.: "Physiology of the Nervous System," New York, Oxford University Press, 1938.

Gasser, H. S., *et al.*: Symposium on the synapse, *J. Neurophysiol.*, 2: 361, 1939.

Gerard, R. W.: Nerve conduction in relation to nerve structure, *Quart. Rev. Biol.*, 6: 59, 1931.

Hardesty, I.: On the development and nature of neuroglia, *Am. J. Anat.*, 3: 229, 1904.

Harrison, R. G.: Further experiments on the development of the peripheral nerves, *Am. J. Anat.*, 5: 121, 1906.

———: Neuroblast versus sheath cell in the development of peripheral nerves, *J. Comp. Neurol.*, 37: 123, 1924.

Hinsey, J.: The innervation of skeletal muscle, *Physiol. Rev.*, 14: 514, 1934.

Hoerr, N. L.: Cytological studies by Altmann-Gersh freezing-drying method. III. The pre-existence of neurofibrillae and their disposition in the nerve fiber, *Anat. Record*, 66: 81, 1936.

———: IV. The structure of the myelin sheath of nerve fibers, *Anat. Record*, 66: 91, 1936.

Kuntz, A.: The sympathetic nerve cells, in Cowdry's "Special Cytology," 3: 1423, 1932.

———: "The Autonomic Nervous System," Philadelphia, Lea & Febiger, 1945.

Langworthy, O. R.: General principles of autonomic innervation, *Arch. Neurol. & Psychiat.*, 50: 590, 1943.

Malone, E. F. The general relation of histological character to function in mammalian neurons, in Cowdry's "Special Cytology," 3: 1405, 1932.

Parker, G. H.: The neurofibril hypothesis, *Quart. Rev. Biol.*, 4: 155, 1929.

Penfield, W. Neuroglia and microglia. The interstitial tissue of the central nervous system, in Cowdry's "Special Cytology," 3: 1417, 1932.

Ranson, S. W.: Non-medullated nerve fibers in the spinal nerves, *Am. J. Anat.*, 12: 67, 1911.

——: "The Anatomy of the Nervous System," Philadelphia, W. B. Saunders *Company*, 1913

Speidel, C. C.: Studies of living nerves. II Activities of amoeboid growth cones sheath-cells, and myelin segments, as revealed by prolonged observations of individual nerve fibers in frog tadpoles, *Am. J. Anat.*, 52: 1, 1933.

——: III. Phenomena of nerve irritation and recovery, degeneration and repair, *J. Comp. Neurol.*, 61: 1, 1935.

Weiss, P., and H. Wang: Neurofibrils in living ganglion cells of the chick, cultivated in vitro, *Anat. Record*, 67: 105, 1936.

Windle, W., and S. L. Clark: Observations on the histology of the synapse, *J. Comp. Neurol.*, 46: 153, 1928.

Wislocki, G. B.: Cytology of the cerebro-spinal pathway, in Cowdry's "Special Cytology," 3: 1185, 1932.

Wood, L. H.: Certain anatomical and physiological aspects of the meninges and cerebrospinal fluid, *Brain*, 58: 383, 1935.

10. VASCULAR ORGANS

Bensley, R. R., and B. J. Vimtrup.: On the nature of the Rouget cells of the capillaries, *Anat. Record*, 39: 37, 1928.

Bremer, J. L.: An interpretation of the development of the heart, *Am. J. Anat.*, 42: 307, 1928.

Chambers, R., *and B. W. Zweifach: Capillary endothelial cement in relation to* permeability, *J. Cellular & Comp. Physiol.*, 15: 255, 1940.

——: Topography and function of the mesenteric capillary circulation, *Am. J. Anat.*, 75: 173, 1944.

Clark, E. R.: Arterio-venous anastomoses, *Physiol. Rev.*, 18: 229, 1938.

——: *Growth and development of blood vessels and lymphatics, Ann. Internal Med.*, 9: 1043, 1936.

Clark, E. R., and E. L. Clark: Microscopic observations on the extra-endothelial cells of living mammalian blood vessels, *Am. J. Anat.*, 66: 1, 1940.

DeWitt, L. M.: Observations on the sino-ventricular connecting system of the mammalian heart, *Anat. Record*, 3: 475, 1909.

Hollingshead, W. H.: A cytological study of the carotid body of the cat, *Am. J. Anat.*, 73: 185, 1943.

McClure, C. F. W., The endothelial problem, *Anat. Record*, 22: 219, 1921.

Nonidez, J. F.: The aortic (depressor) nerve and its associated epithelioid body, the glomus aorticum, *Am. J. Anat.*, 57: 259, 1935.

Schmidt, C. F., and J. H. Comroe, Jr.: Functions of the carotid and aortic bodies, *Physiol. Rev.*, 20: 115, 1940.

Todd, T. W.: The specialized systems of the heart, in Cowdry's "Special Cytology," 2: 1173, 1932.

LYMPHATICS

Clark, E. R., and E. L. Clark: Further observations on living lymphatic vessels in the transparent chamber in the rabbit's ear—their relation to the tissue spaces, *Am. J. Anat.*, 52: 273, 1933.

Conway, E. A.: Cyclic changes in lymphatic nodules, *Anat. Record*, 69: 487, 1937.

Downey, H.: The structure and origin of the lymph sinuses of mammalian lymph nodes and their relations to endothelium and reticulum, *Haematologica*, 3: 31, 1922.

Drinker, C. K., and J. M. Yoffey: "Lymphatics, Lymph, and Lymphoid Tissue. Their Physiological and Clinical Significance," Cambridge, Mass., Harvard University Press, 1941.

Lewis, F. T.: The development of the lymphatic system in rabbits, *Am. J. Anat.*, 5: 95, 1906.

Sabin, F. R.: On the origin of the lymphatic system from the veins, and the development of the lymph hearts and thoracic duct in the pig, *Am. J. Anat.*, 1: 367, 1902.

———: Method of the growth of the lymphatic system, *Harvey Lectures*, 1916.

11. LYMPHOID ORGANS

Conway, E. A.: Cyclic changes in lymphatic nodules, *Anat. Record*, 69: 487, 1937.

Foot, N. C.: The reticulum of the human spleen, *Anat. Record*, 36: 79, 1927.

Kingsbury, B. F. Development of the pharyngeal tonsils (cat): cell types, *Am. J. Anat.*, 51: 269, 1933.

———: The interpretation of thymus bodies, *Endocrinology*, 29: 155, 1941.

Knisely, M. H.: Microscopic observations on the circulatory systems of living transilluminated mammalian spleens, *Proc. Soc. Exp. Biol. & Med.*, 32: 212, 1934.

———: Spleen studies, *Anat. Record*, 65: 23 and 131, 1936.

Krumbhaar, E. B. Functions of the spleen, *Physiol. Rev.*, 6: 160, 1926.

Kyes, P.: The spleen, in Cowdry's "Special Cytology," I: 529, 1932.

MacKenzie, D. W., A. O Whipple, and M. P. Wintersteiner: Studies on the microscopic anatomy and physiology of living transilluminated mammalian spleens, *Am. J. Anat.*, 68: 397, 1941.

Nelson, W. O.: The relation of the thymus and pineal glands to genital functions, "Sex and Internal Secretions" (Allen, Ed.), 1121, 1939.

Ramsey, A. J.: Development of the palatine tonsil, *Am. J. Anat.*, 57: 171, 1935.

Robinson, W. L.. The vascular mechanism of the spleen, *Am. J. Path.*, 2: 341, 1926.

Solnitzky, O.: The Schweigger-Seidel sheath (ellipsoid) of the spleen, *Anat. Record*, 69: 55, 1937.

Thiel, G. A., and H. Downey: The development of the mammalian spleen, with special reference to its hematopoietic activity, *Am. J. Anat.*, 28: 279, 1921.

12. DIGESTIVE ORGANS

Beams, H. W.: Notes on the cytology of the parietal cells of the stomach of the rat, *Anat. Record*, 53: 31, 1932.

Bensley, R. R.: The gastric glands, in Cowdry's "Special Cytology," 1: 199, 1932.

Carlson, A. J.: The secretion of gastric juice in health and disease, *Physiol. Rev.*, 3: 1, 1923.

Ferguson, A. N.: Cytological study of the regeneration of the gastric glands following the experimental removal of large areas of mucosa, *Am. J. Anat.*, 42: 403, 1928.

Florey, H. W., R. D. Wright, and M. A. Jennings: The secretions of the intestine, *Physiol. Rev.*, 21: 36, 1941.

Gage, S. H., and P. A. Fish: Fat digestion, absorption and assimilation in man and animals as determined by the dark-field microscope, and a fat-soluble dye, *Am. J. Anat.*, 34: 1, 1924.

Harvey, B. C. H., and R. R. Bensley: Upon the formation of hydrochloric acid in the foveolae and on the surface of the gastric mucous membrane and the nonacid character of the contents of gland cells and lumina, *Biol. Bull.*, 23: 225, 1912.

Johnson, F. P.: Effects of distension of the intestine upon the shape of villi and glands, *Am. J. Anat.*, 14: 235, 1913.

Klein, S.: Nature of the granule cells of Paneth in the intestinal glands of mammals, *Am. J. Anat.*, 5: 315, 1906.

Macklin, C. C., and M. T. Macklin: *The intestinal epithelium, in Cowdry's* "Special Cytology," 1: 233, 1932.

THE TEETH

Noyes, F.: "Dental Histology and Embryology." Philadelphia, Lea & Febiger, 1938.

Orban, B.: "Dental Histology and Embryology." 2d ed., Philadelphia, The Blakiston Company, 1929.

Schour, I.: The Teeth, in Cowdry's "Special Cytology," 1: 69, 1932.

13. GLANDS ASSOCIATED WITH THE DIGESTIVE SYSTEM

Beams, H. W.: Golgi apparatus, canalicular apparatus, vacuome and mitochondria in the islets of Langerhans of the albino rat, *Anat. Record*, 45: 27, 1930.

Beams, H. W., and R. L. King: The origin of binucleate and large mononucleate cells in the liver of the rat, *Anat. Record*, 83: 281, 1942.

Bensley, R. R.: Observations on the salivary glands of mammals, *Anat. Record*, 2: 105, 1908.

——: Studies on the pancreas of the guinea pig, *Am. J. Anat.*, 12: 297, 1911.

Bloom, W.: A new type of granular cells in the islets of Langerhans of man, *Anat. Record*, 49: 363, 1931.

Boyden, E. A.: An analysis of the reaction of the human gallbladder to food, *Anat. Record*, 40: 147, 1928.

Corner, G. W.: Structural units and growth of the pancreas of the pig, *Am. J. Anat.*, 16: 207, 1914.

Forsgren, E.: The anatomical qualities of the liver during the various stages of its functional activities, *J. Morphol.*, 47: 519, 1929.

Halpert, B.: Morphological studies on the gallbladder. II. The "True Luschka Ducts" and "Rokitansky-Aschoff Sinuses" of the human gallbladder, *Bull. Johns Hopkins Hosp.*, 41: 77, 1927.

Ivy, A. C.: The physiology of the gallbladder, *Physiol. Rev.*, 14: 1, 1934.

Lee, F. C.: On the lymph vessels of the liver, Contrib. to Embryol., *Carnegie Inst. of Wash. Pub.*, No. 74, 65, 1925.

O'Leary, J. L.: An experimental study on the islet cells of the pancreas in vivo, *Anat. Record*, 45: 27, 1930.

Opie, E. L.: Cytology of the pancreas, in Cowdry's "Special Cytology," 1: 373, 1932.

Stormont, D. L.: The salivary glands, in Cowdry's "Special Cytology," 1: 153, 1932.

Wharton, G. K.: Blood supply of the pancreas with special reference to that of the islands of Langerhans, *Anat. Record*, 53: 55, 1932.

14. THE RESPIRATORY ORGANS

Bensley, R. D., and S. H. Bensley: *Studies of the lining of the pulmonary alveolus* of the normal lungs of adult mammals, *Anat. Record*, 64: 41, 1936.

Bremer, J. L.: *Postnatal development of alveoli in the mammalian lung in relation* to the problem of the alveolar phagocyte, Contrib. to Embryol., *Carnegie Inst. of Wash. Pub.*, 25: 85, 1935.

Foot, N. C.: Studies on endothelial reactions. X. On the origin of pulmonary "dust cells," *Am. J. Path.*, 3: 413, 1927.

Fried, B. M.: The lungs and the macrophage system, *Arch. of Path.*, **17**: 76, 1934.

Ham, A. W., and K. W. Baldwin: A histological study of the development of the lung with particular reference to the nature of alveoli, *Anat. Record*, **81**: 363, 1941.

Larsell, O., and R. S. Dow: The innervation of the human lung, *Am. J. Anat.*, **52**: 125, 1933.

Macklin, C. C.: The musculature of the bronchi and lungs, *Physiol. Rev.*, **9**: 1, 1929.

———: Pulmonic alveolar epithelium. A round table conference, *J. Thoracic Surg.*, **6**: 82, 1936.

Miller, W. S.: Epithelium of the lower respiratory tract, in Cowdry's "Special Cytology," **1**: 132, 1932.

———: "The Lung," *Springfield, Ill., Charles C Thomas*, 1937.

Ogawa, C.: The finer ramifications of the human lung, *Am. J. Anat.*, **27**: 315, 1920.

Robertson, O. H.: Phagocytosis of foreign material in the lung, *Physiol. Rev.*, **21**: *112, 1941.*

Schaeffer, J. P.: The mucous membrane of the nasal cavity and the paranasal sinuses, in Cowdry's "Special Cytology," **1**: 105, 1932.

Stewart, F. W.: A histogenic study of the respiratory epithelium, *Anat. Record*, **25**: 181, 1923.

15. THE URINARY ORGANS

Bensley, R. R., and R. D. Bensley: The structure of the renal corpuscle, *Anat. Record*, **47**: 147, 1930.

Cushny, A. R.: "The Secretion of Urine," London & New York, Longmans Green & Company, 1926.

Edwards, J. G.: Studies of aglomerular and glomerular kidneys, *Am. J. Anat.*, **42**: 75, 1928.

———: The vascular pole of the glomerulus in the kidney of vertebrates, *Anat. Record*, **76**: 381, 1940.

Holton, S. G., and R. R. Bensley: The functions of the differentiated parts of the uriniferous tubule in the mammal, *Am. J. Anat.*, *47: 241, 1931.*

Huber, G. C.: Renal tubules, in Cowdry's "Special Cytology," **2**: 933, 1932.

MacCallum, D. B.: The bearing of degenerating glomeruli on the problem of the *vascular supply of the mammalian kidney, Am. J. Anat., 65: 69, 1939.*

Marshall, E. K., Jr.: The comparative physiology of the kidney in relation to theories of renal secretion, *Physiol. Rev.*, **14**: 133, 1934.

Richards, A. N.: "*Methods and Results of Direct Investigations of the Function of* the Kidney," Baltimore, The Williams & Wilkins Company, 1929.

———: Recent developments in the experimental study of the functions of the kidney, *Arch. of Path.*, **13**: 847, 1932.

Shannon, J. A.: Renal tubular excretion, *Physiol. Rev.*, **19**: 63, 1939.

Smith, H. W.: Physiology of the renal circulation, *The Harvey Lectures*, **34**: 1940.

16. THE DUCTLESS GLANDS

Allen, E. (editor): "Sex and Internal Secretions," 2d ed., Baltimore, The Williams & Wilkins Company, 1939.

Atwell, W.: Development of the hypophysis cerebri in man, with special reference to the pars tuberalis, *Am. J. Anat.*, **37**: 159, 1926.

Bailey, P.: Structure of the hypophysis cerebri of man and of the common laboratory *animals, in Cowdry's "Special Cytology," 2: 771, 1932.*

———: The pineal body, in Cowdry's "Special Cytology," **2**: 787, 1932.

Bennett, H. S.: Cytological manifestations of secretion in the adrenal medulla of the cat, *Am. J. Anat.*, 69: 333, 1941.

Bensley, R. R.: *Normal mode of secretion in the thyroid gland, Am. J. Anat.*, 19: 37, 1916.

Boyd, J. D.: The development of the human carotid body, Contrib. to Embryol., *Carnegie Inst. of Wash. Pub.*, 26: 3, 1937.

Cowdry, E. V.: Reticular material as an indicator of physiologic reversal in secretory *polarity in the thyroid cells of the guinea pig, Am. J. Anat.*, 30: 25, 1922.

———: Anatomy, embryology, comparative anatomy and histology of the parathyroid, *Endocrin. & Metabol.*, 1: 501, 1940.

Deanesley, R.: Experimental studies on the histology of the mammalian thymus, *Quart. J. Microscop. Sci.*, 72: 247, 1929.

DeRoberts, E.: The cytology of the parathyroid gland of rats injected with parathyroid extract, *Anat. Record*, 78: 473, 1940.

Evans, H. M.: The function of the anterior hypophysis, *The Harvey Lectures*, 1924.

Evans, H. M., K. Korpi, M. E. Simpson, R. I. Pencharz, and D. H. Wonder: On the separation of the interstitial cell-stimulating, luteinizing, and follicle-stimulating fractions in the anterior pituitary gonadotropic complex, *Univ. of Cal. Pub. in Anat.*, 1: 255, 1936.

Evans, H. M., and M. E. Simpson: Reduction of the thymus by gonadotropic hormone, *Anat. Record*, 60: 423, 1934.

Gersh, I.: The structure and function of the parenchymatous glandular cells in the neurohypophysis of the rat, *Am. J. Anat.*, 64: 407, 1939.

Gladstone, R. J., and C. P. G. Wakeley: "The Pineal Organ," Baltimore, The Williams & Wilkins Company, 1940.

Hoerr, N.: The cells of the suprarenal cortex in the guinea pig. Their reaction to injury and their replacement, *Am. J. Anat.*, 48: 139, 1931.

Houssay, B. A.: Certain relations between parathyroids, hypophysis, and pancreas, *The Harvey Lectures*, *31: 116, 1936.*

Jackson, C. M.: The postnatal development of the suprarenal gland and the effects of inanition upon its growth and structure in the albino rat, *Am. J. Anat.*, 25: 221, 1919.

Jordan, H. E., and G. W. Horsley: The significance of the concentric corpuscles of Hassall, *Anat. Record*, 35: 279, 1927.

Keene, M. F. L., and E. E. Hewer: Observations of the development of the human suprarenal gland, *J. Anat.*, 61: 302, 1927.

Kingsbury, B. F.: The term "chromaffin system" and the nature of the "chromaffin reaction," *Anat. Record*, 5: 11, 1911.

Koch, F. C.: The male sex hormones, *Physiol. Rev.*, 17: 153, 1937.

Lewis, D., and F. C. Lee: On the glandular elements in the posterior lobe of the human hypophysis, *Bull. Johns Hopkins Hosp.*, 41: 241, 1927.

Marine, D.: The thyroid, parathyroids and thymus, in Cowdry's "Special Cytology,' 2: 797, 1932.

Moore, C. R., and D. Price: Gonad hormone functions, and the reciprocal influence between gonads and hypophysis with its bearing on the problem of sex-hormone antagonism, *Am. J. Anat.*, 50: 13, 1932.

Morgan, J. R. E.: The parathyroid glands, Arch. of Path., 21: *10, 1936.*

Norris, E. H. Morphogenesis of the follicles in the human thyroid gland, *Am. J. Anat.*, 20: 411, 1916.

———: The parathyroid glands and the lateral thyroid in man: their morphogenesis, histogenesis, topographic anatomy and prenatal growth, Contrib. to Embryol., *Carnegie Inst. of Wash. Pub.*, 26: 249, 1937.

Rasmussen, A. T.: Ciliated epithelium and mucus-secreting cells in the human hypophysis, *Anat. Record*, 41: 273, 1929.

———: Origin of the basophilic cells in the posterior lobe of the human hypophysis, *Am. J. Anat.*, 46: 461, 1930.

———: Percentage of the different types of cells in the anterior lobe of the hypophysis in the adult human female, *Am. J. Path.*, 9: 459, 1933.

Riddle, O.: Endocrine aspects of the physiology of reproduction, *Ann. Rev. Physiol.*, 3: 573, 1941.

Rogoff, J. M.: The suprarenal bodies, in Cowdry's "Special Cytology," 2: 869, 1932.

Severinghaus, A. E.: Cellular changes in the anterior hypophysis with special reference to its secretory activities, *Physiol. Rev.*, 17: 556, 1937.

Van Dyke, J. H.: On the origin of accessory thymus tissue, Thymus IV: The occurrence in man, *Anat. Record*, 79: 179, 1941.

Welsh, D. A.: Concerning the parathyroid glands: a critical, anatomical, and experimental study, *J. Anat. & Physiol.*, 32: 293, 380, 1898.

17. THE SKIN

Becker, S. W.: Melanin pigmentation, *Arch. Dermatol. & Syphilol.*, 16: 259, 1927.

Cowdry, E. V.: The skin, in Cowdry's "Special Cytology," 1: 3, 1932.

Danforth, C. H.: Physiology of human hair, *Physiol. Rev.*, 19: 94, 1939.

Loeb, Leo: The cytology of the mammary gland, in Cowdry's "Special Cytology," 3: 1631, 1932.

Nelson, W. O.: Endocrine control of the mammary gland, *Physiol. Rev.*, 16: 488, 1936.

Strong, R. M.: Color of the skin and corium pigmentation, *Arch. of Path.*, 3: 938, 1927.

Trotter, Mildred: The hair, in Cowdry's "Special Cytology," 1: 41, 1932.

Weatherford, H. L.: A cytological study of the mammary gland, *Am. J. Anat.*, 44: 199, 1929.

18. MALE ORGANS OF REPRODUCTION

Allen, E.: "Sex and Internal Secretions," Baltimore, The Williams & Wilkins Company, 1939.

Arey, L. B.: New diagrams illustrating the transformation period of the human spermatid as prepared by the late Professor Bowen, *Anat. Record*, 47: 31, 1930.

Bremer, J. L.: Morphology of the tubules of the human testis and epididymis, *Am. J. Anat.*, 11: 393, 1911.

Gatenby, J. B., and H. W. Beams: The cytoplasmic inclusions in the spermatogenesis of man, *Quart. J. Microscop. Sci.*, 78: 1, 1935.

Curtis, G. M.: Morphology of the mammalian seminiferous tubule, *Am. J. Anat.*, 24: 339, 1918.

Koch, F. C.: The male sex hormone, *Physiol. Rev.*, 17: 153, 1937.

Lowsley, O. S.: Development of the human prostate gland, *Am. J. Anat.*, 13: 299, 1912.

Macklin, C. C., and M. T. Macklin: The seminal vesicles, prostate and bulbourethral glands, in Cowdry's "Special Cytology," 3: 1771, 1932.

Metz, C. W.: The male germ cells, in Cowdry's "Special Cytology," 3: 1727, 1932

Moore, C. R.: Biology of the testes, in "Sex and Internal Secretions" (Allen, ed.), Baltimore, The Williams & Wilkins Co., 1939.

Moore, R. A.: The evolution and involution of the prostate gland, *Am. J. Path.*, 12: 599, 1936.

Painter, T. S.: Studies in mammalian spermatogenesis, *J. Exp. Zoöl.*, 37: 291, 1923.

Pollock, W. F.: Histochemical studies of the interstitial cells of the testis, *Anat. Record*, 84: 23, 1942.

Rasmussen, A. T.: Interstitial cells of the testis, in Cowdry's "Special Cytology," 3: 1673, 1932.

Riddle, O.: Factors in the development of sex and secondary sexual characteristics, *Physiol. Rev.*, 11: 63, 1931.

———: Endocrine aspects of the physiology of reproduction, *Ann. Rev. Physiol.*, 3: 573, 1941.

Watson, E. M.: Development of the seminal vesicles in man, *Am. J. Anat.*, 24: 395, 1918.

19. FEMALE ORGANS OF REPRODUCTION

Allen, E., J. P. Pratt, Q. U. Newell, and L. J. Bland: Human ova from large follicles: including a search for maturation divisions and observations on atresia, *Am. J. Anat.*, 46: 1, 1930.

Baker, B. L., S. Hook, and A. E. Severinghaus: The cytological structure of the human chorionic villus and decidua parietalis, *Am. J. Anat.*, 74: 291, 1944.

Bartelmez, G. W.: Histological studies on the menstruating mucous membrane of the human uterus, Contrib. to Embryol., *Carnegie Inst. of Wash. Pub.*, No. 142, 24: 141, 1933.

———: Menstruation, *Physiol. Rev.*, 17: 28, 1937.

Bartelmez, G. W., and C. M. Bensley: Human uterine gland cells, in Cowdry's "Special Cytology," 3: 1523, 1932.

Corner, G. W.: Cytology of the ovum, ovary, and Fallopian tube, in Cowdry's "Special Cytology," 3: 1565, 1932.

Dodds, G. S.: The area of the chorionic villi in the full term placenta, *Anat. Rec.*, 24: 287, 1922.

Jones, G. E., G. O. Gey, and M. K. Gey: Hormone production by placental cells maintained in continuous culture, *Bull. Johns Hopkins Hosp.*, 72: 26, 1943.

Kingsbury, B. F.: The interstitial cells of the mammalian ovary: Felis domestica, *Am. J. Anat.*, 16: 59, 1914.

Long, J. A., and H. M. Evans: The oestrus cycle in the rat and its associated phenomena, Mem. Univ. Calif., 6: 1922.

Markee, J. E.: Menstruation in endometrial transplants in the rhesus monkey, Contrib. to Embryol., *Carnegie Inst. of Wash. Pub.*, No. 177, 28: 221, 1940.

O'Leary, J. L.: Form changes in the human uterine gland during the menstrual cycle and in early pregnancy, *Am. J. Anat.*, 43: 289, 1929.

Papanicolaou, G. N.: The sexual cycle in the human female as revealed by vaginal smears, *Am. J. Anat.*, 52: 519, 1933.

Snyder, F. F.: Changes in the human oviduct during the menstrual cycle and pregnancy, *Bull. Johns Hopkins Hosp.*, 35: 141, 1924.

Traut, H. F., Bloch, P. W., and A. Kuder: Cyclical changes in the human vaginal mucosa, *Surg. Gynecol. & Obstet.*, 63: 7, 1936.

20. THE EYE

Arey, L. B.: Retina, choroid and sclera, in Cowdry's "Special Cytology," 3: 1213, 1932.

Detweiler, S. R.: "Vertebrate Photoreceptors," New York, The Macmillan Co., 1943

Duke-Elder, W. S.: "Recent Advances in Ophthalmology," 3d ed., Philadelphia, The Blakiston Company, 1934.

Hecht, S.: Rods, cones, and the chemical basis of vision, *Physiol. Rev.*, 17: 239, 1937.

Mann, Ida C.: The cornea and the lens, in Cowdry's "Special Cytology," 3: 1307, 1932.

Polyak, S.: "The Retina," *Chicago, University of Chicago Press,* 1911.

Salzman, M. "The Anatomy and Histology of the Human Eyeball in the Normal State," Trans. by E. V. L. Brown, Chicago, University of Chicago Press, 1912.

Walls, G. L.: Human rods and cones, *Arch. of Ophthalmol.,* 12: 914, 1931.

21. THE EAR

Bast, T. H.: Development of the otic capsule, *Arch. Otolaryngol.,* 16: 19, 1932.

Bowen, R. E.: The cupula of the membranous labyrinth, *J. Comp. Neurol.,* 58: 517, 1933.

Guild, S. R., *et al.:* Correlation of differences in the density of innervation of the organ of Corti with differences in acuity of hearing, *Acta. Oto-Laryngol.,* 15: 269, 1931.

Maxwell, S. S.: "The Labyrinth and Equilibrium," Philadelphia, J. B. Lippincott, 1923.

Shambaugh, G. E.: Cytology of the internal ear, in Cowdry's "Special Cytology," 3: 1335, 1932.

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